

Technology Assessment And Setting Priorities For The Adoption On A National Level - The Israeli Experience

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The Israeli Health System

Introduction

Israel's healthcare system is considered to be an advanced system including a broad spectrum of publicly funded sophisticated medical technologies, such as organ transplants, in-vitro fertilization, high-tech imaging techniques, and the latest developed pharmaceuticals.

The Israeli healthcare system has reached a high standard of medical care, and adopts medical technologies rather early. The Israeli healthcare system is also considered to be a rapid adopter of health technologies into its publicly funded health services basket (HSB). Examples for early adoption to the HSB include Herceptin^R for metastatic breast cancer in 2000 (in comparison to adoption by NICE in 2002, by Medicare in 1999 and by the Australian authorities in 2001) and Photodynamic therapy for age related macular degeneration in 2001 (in comparison to NICE in 2003, Medicare in 2004 and the Australians in 2001). It is worth mentioning that Herceptin as adjuvant treatment of early breast cancer was included in the HSB in 2006, only months after its registration in the USA.

Despite the extensive range of publicly funded health services, the Israeli population expects and demands a rapid public funding of new and innovative technologies (both drugs and devices that have only recently been registered in the world, sometimes even before their registration in Israel) while using both the justice system, the political system and the media to achieve their goal.

The social and professional demand for new and expensive technologies to be provided by the government is continuously increasing. Lobbying for new technologies has become a trend; for example pharmaceutical companies or patient interest groups ask politicians for their support or use the media to publicize the technology and their cause.

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The National Health Insurance Law (NHIL)

In 1995, as part of a major reform in the Israeli healthcare system, the National Health Insurance Law was enacted, thus making health insurance both compulsory and universal. The law determined a basic list of health services ("health services basket" - HSB) to which all residents are entitled. The government is responsible for funding those health services, while the Health Funds (numbering 4) are responsible for their provision. The law also specifies that all health services included in the HSB will be of reasonable quality within the framework of the funding sources available.

Extent of the HSB

The HSB was defined as the 1994 formulary of Israel's largest Health Fund, Clalit, that insured at the time approximately two thirds of the population and currently insures more than half of the Israeli population. This list included drugs, devices, procedures and health services.

Currently the HSB includes over 3,500 Medical technologies and services – 2/3 of which are medications.

The annual cost in 2006 of providing all services included in the HSB for the entire Israeli population (about 7 million people) is approximately 6 billion US dollars.

Updating the HSB

The law determines an annual update of the total cost of the HSB by two fixed coefficients – one reflecting demographic changes and one reflecting the aging of the population. However, the NHIL does not include a coefficient for technological advances and determines that the HSB can be technologically updated only by an additional budget allocation from the Ministry of Finance, traditionally once a year as part of the Annual State Budget Act, which is approved by Parliament (around January of each year).

For three consecutive years, between the enactment of the NHIL in January 1995 and December 1997, the HSB was not updated, since no financial resources were allocated for its update.

In December 1997, after a considerable public outcry, the Ministry of Finance allocated 42 million US dollars for updating the HSB, although according to the health technology factor, estimated at an annual 2% of the HSB, the annual budgetary allocation for updating the HSB should have been at the time around 90 million US dollars.

Since the December 1997 update the HSB has been annually updated, except for the year of 2003. The budgetary allocation differed from year to year ranging from 14 to 157 million US dollars (Complete data presented in table 1).

Table 1:

Year	Budget allocation (in million US \$ (% of total HSB))	Number of technologies added		
		Total	Drugs	Other technologies
1998	42 million US \$ (0.9%)	17	17	-
1999	37 million US \$ (0.83%)	54	47	7
2000	61 million US \$ (1.32%)	128	105	23
2001	48 million US \$ (0.95%)	84	75	9
2002	32 million US \$ (0.71%)	61	53	8
2003	0	-	-	-
2004	14 million US \$ (0.27%)	35	32	3
2005	88 million US \$ (1.63%)	69	52	17
2006	157 million US \$ (2.88%)	75	64	11

The Medical Technology Administration

Over the years the HSB updates, regardless of the extent of the allocated budget, were performed by a similar process performed by the Medical Technology Administration (MTA) at the Israeli Ministry of Health.

The MTA was established in 1998. Among the MTA's areas of responsibility are:

1. National policy for medical technologies (Medications, medical devices, apparatus, medical procedures and the organization of frameworks such as additional hospital beds)
2. Regulation, registration and licensing of medical technologies
3. Management and update of the HSB.

The MTA developed and implemented a mechanism for updating the HSB, based on health technology assessment tools integrated with priority setting on a national level.

We decided to take a systematic approach of Health Technology Assessment (HTA), based on a model suggested by Shemer and Siebzehner (Figure 1). According to this model, each technology is assessed by a comprehensive process, which includes the evaluation of evidence-based clinical, epidemiological and economic aspects. In order for the mechanism to be practical and feasible, combined with the reality of limited resources, the model also integrates social, legal and ethical aspects.

The Israeli updating mechanism of the HSB

The different stages of the proposed mechanism for the update of the HSB can be briefly described as follows:

1. Identifying the new proposed technologies.
2. Quick assessment and initial screening.
3. Comprehensive assessment – including an extended data collection and consultation with National Advisory Councils and the Israeli Medical Association.
4. Priority setting by the Ministry of Health and recommendations to the Public Committee.
5. Decision-making by the Public Committee, based on the MTA's assessments and recommendations.
6. Government approval and legislation.
7. Provision of the approved new technologies by the Health Funds and Hospitals.

Since the update of the HSB is linked to the annual budget, the process is designed to be performed in one year cycles.

Identification of new technologies

A circular is published on the Ministry of Health's website and is sent as well to all Health Funds directors, hospital directors, chairpersons of the National Advisory Councils, the Israeli Medical Association and Health Ministry units. Moreover, the process is also published in the mass media. The circular specifies the mechanism and time table for applications to add new technologies to the HSB (See attached appendix A – example of guidelines for the submission of a request to include a new medical technology in the HSB by medical technologies companies).

Submitting applications is open to everyone - professional bodies, patient interest groups, politicians, pharmaceutical companies, etc. At the same time the MTA actively identifies significant technologies needed to be included in the HSB using different sources such as the annual report of the NHIL's Ombudsman, in-house screening of the National Drug Registry, important issues relevant to the Health Ministry's agenda and so forth.

Following that, a list of approximately 400 health technologies proposed for inclusion in the HSB, is formed each year.

Quick assessment and initial screening

Since the list of proposed technologies contains about 400 different proposals, a comprehensive evaluation can not be conducted for all the technologies. Moreover due to the limited number of professional staff designated for performing HTAs (numbering 7 - including medical doctors, clinical pharmacists and registered nurses) combined with obvious time constraints, a quick assessment and initial screening is performed.

The quick assessment includes reviewing, completing and correcting the submitted application, a brief data collection – including a literature search, review of the regulatory status, summary of efficacy and safety, a short needs assessment and an examination of the clinical experience with the technology both in Israel and abroad . The initial screening uses different criteria enabling a quick mechanism for discarding technologies deemed inappropriate for the HSB update. For example – drugs or medical devices not registered by the Ministry of Health are usually not considered eligible for inclusion in the HSB. Moreover, even though a technology passes the hurdles of efficacy and safety, it will not necessarily be considered for the update if it

does not have the specific characteristics of the HSB. For example, a new technology which is part of the infrastructure of a hospital (e.g. navigation system for neurosurgery) will not be considered appropriate for the HSB update but will rather be referred to be included as part of a technological coefficient for hospitals. Another example is a technology improving professional standards though not contributing to a major change in the quality of treatment.

Comprehensive assessment

The comprehensive assessment is aimed to broaden and refine the assessments of the technologies deemed eligible for inclusion in the HSB. The comprehensive assessment also addresses issues that were not included in the initial assessment such as a techno-epidemiological evaluation, the economic burden on the individual and the health system, coverage and reimbursement in other countries.

The sources of data used for performing the assessments include scientific literature, Health Ministry's databases, expert's opinions, Health Funds databases regarding utilization of medical technologies, the original proposals and other relevant data sources. Costs are obtained from the Health Ministry's databases, the manufacturer of the relevant technology, the hospitals and the Health Funds.

The clinical, epidemiological and economic evaluations are performed simultaneously.

The major role of the **clinical evaluation** is to assess the clinical importance of the suggested technology in comparison to existing treatments for an indicated disease-state. The evaluation is based on the most updated available data and includes evidence-based data, post-marketing effectiveness data, commonly used treatment regimens of the technology, frequent and significant adverse events. Alternative treatments are identified and compared to the proposed technology. Attention is given to the issue of identifying specific patient groups that might benefit mostly from the use of the technology, in case public reimbursement would not be feasible for the entire patient population.

The **epidemiological evaluation** includes incidence, prevalence, mortality and morbidity data from Israel and abroad, where available. The number of patients to be treated by a specific technology is estimated in a "tailor made" fashion intergating the epidemiological indices with data from scientific literature, practicing physicians, pharmaceutical companies and Health Funds.

Until recently, the **economic evaluation** has been performed based on a cost-effectiveness approach with cost utility data, when available. The overall cost is calculated as the product of the cost of the annual treatment per patient and the number of patients estimated to use it each year. The cost of an annual treatment per patient is based on the net cost of the treatment regimen or distribution of several treatment regimens - i.e. minus the cost of an annual treatment with the currently available treatment in the HSB and possible savings in health resources.

Currently the Ministry of Health is considering a mandatory addition of cost utility information to the economic evaluation.

In this stage of the comprehensive assessment the MTA uses both internal and external bodies to assist and enrich the completion of the assessment. Such bodies of reference include the National Advisory Councils (NACs) and the Israeli Medical Association (IMA) for clinical issues.

The NACs are professional multi-disciplinary committees, numbering 20-25 members (all voluntary), appointed by the General Director of the Ministry of Health in order to advise to the Ministry of Health on issues of prevention, diagnosis and treatment in various clinical fields. There are about 20 NACs encompassing such fields as Oncology, Heart disease, Pediatrics, Geriatrics, Imaging, Trauma and so forth.

The MTA divides the list of proposed technologies by fields of specialty. The relevant sub-list is sent to the appropriate NAC and professional association of the IMA. In turn they are requested to grade each proposed technology according to two sets of scales – A scale reflecting the extent of diffusion and acceptance of the technology by the healthcare system (the “adoption” scale) and a scale of priority.

The adoption scale awards each technology with one of the following grades:

- 1 Standard of care with extensive clinical use
- 2 Standard of care with limited clinical use
- 3 Known as a therapeutic alternative
- 4 Experimental or not in use

According to the priority scale each technology is graded as one of the following:

- 1 Vital for inclusion in the HSB
- 2 Important for inclusion in the HSB
- 3 Possible inclusion in the HSB ('Nice to have')
- 4 Not recommended for inclusion in the HSB

Each NAC or professional association of the IMA appoints a subcommittee for technology advances and clinical priority setting. The subcommittee presents its findings for discussion and decision making at the general meetings of the specific NAC / professional association.

For issues regarding pricing and economic evaluations the MTA collaborates with the Budgetary Department at the Ministry of Health and operates a technoepidemiology subcommittee comprising of representatives from the MTA, Ministry of Health, Ministry of Finance and the Health Funds.

Priority setting by the Ministry of Health

The completed assessments performed by the MTA are passed to the Medical Technology Forum for a final evaluation. The Medical Technology Forum is an inner forum of the Ministry of Health, chaired by the Director General of the Ministry and made up of the senior management of the Ministry of Health and MTA personnel.

The proposed technologies are prioritized by the Medical Technology Forum by a scale from 1 to 10 and a placement into three major categories of importance:

- Group A - High priority technologies (graded 8-10);
- Group B - Intermediate priority technologies (graded 4-7);
- Group C - Low priority technologies (graded 1-3).

Priorities are set according to an established guiding criteria, which include the effect of the suggested technologies on mortality, morbidity, longevity and quality of life, existence of alternative treatments, the number of possible patients to benefit from the technology, the cost of the technology and its affordability both by society and by the individual patient.

No scoring method is used for the above-mentioned criteria. Each Forum member is aware of the criteria for setting priorities, and based on those criteria and on the comprehensive assessment, decides on the recommended priority. The entire process leads to a final list of recommended technologies for inclusion in the HSB, ranked according to priority.

It is worth mentioning that technologies ranked as high priority, number usually 150-200 technologies .

The Ministry of Health's recommendations, with the final comprehensive assessments for each technology, are submitted to the public committee for the update of the HSB to be used as the background material for its discussions.

Decision-making

A public committee appointed by the Minister of Health and the Minister of Finance (and approved by the NIHL Health Council), made up of representatives from the government, the Health Funds and the public, evaluates each technology, based on the analysis performed by the Ministry of Health, and decides which technologies will be added to the HSB.

The choice of the committee members is purposely designed to make sure that decisions would be based on national considerations (and not on individual organization's preferences), that the public / patients' perspective will be heard as well as the perspective of healthcare professionals and that the committee's decisions will be feasible.

The committee numbers 24 members - 3 from the Ministry of Health, 4 from the Health Funds (one for each Health Fund), 2 from public hospitals, 2 from the Israeli Medical Association, 1 from the Ministry of Finance, 3 Health Economists, 9 Public representatives from the fields of medical sciences, ethics, social sciences and welfare.

The committee reviews all the proposed technologies and, using a set of guiding criteria, initially selects the technologies deemed to be further discussed.

Examples for the criteria used are:

- Life saving technology with full recovery.
- The potential of the technology to prevent mortality / morbidity.
- The number of patients to benefit from the use of technology.
- The financial burden on society and the individual patient.
- Technology which leads to an increase in longevity as well as quality of life.
- Technology of which the net gain to the health care system or to society is higher than its cost in a short / long term perspective.
- Mutual assistance for publicly funding a very expensive technology (of proven efficacy) to the individual, yet of reasonable cost to society.

The work of the committee is very sensitive and complex. The committee faces dilemmas such as "much for few vs. little for many", what can be defined as a "life-saving" technology and urgent health needs vs investment in future health. The committee prioritizes the selected technologies using the A10-C1 scale. The committee uses a consensus decision model – i.e. all decisions are made unanimously. The priority of each technology is agreed by all members and no voting or scoring method is being used. The committee holds numerous discussions (closed to the public) spanning about 4 months each year, and concludes its work by recommending, according to the budget allocated by the Ministry of Finance, which technologies should be added to the HSB and for which indications/target populations. It is possible to attach directions to specific technologies varying from giving authorization to prescribe only to specialists to a set of clinical guidelines according to which treatment will be reimbursed. These directions are set in order to ensure a rational and cost-effective use of each technology, due to budget constraints.

Another group of technologies termed "no cost technologies" is identified as bearing no additional cost compared to existing technologies in the HSB. These technologies are recommended to be included, regardless of their ranking.

Government approval and legislation

The committee recommends a list of technologies for inclusion in the HSB in accordance with the allocated budget. The committee also ranks an additional list of important technologies for which the budget is not sufficient.

After the adoption of said recommendations by the Ministers of Health and Finance and NIHL Health Council, the committee's recommendations are presented for a government approval.

Following the approval by the government the list is presented to the health system and public by a circular from the Director General of the Ministry of Health as well press releases. The new technologies are also officialy added to the list of health services in the NIHL.

Implementation of the new technologies is done rapidly, on account of the Health Funds active participation in the updating process.

Issues in managing and updating the HSB

Over the past 10 years, since the enactment of the NIHL, many dilemmas have emerged and experience was gained regarding issues of managing and updating the Israeli HSB.

Examples of these dilemmas include, among others:

- A. How to define a new technology for the HSB ?
 - Should a combination of 2 existing technologies be considered a new technology ?
 - What is the breakpoint between natural evolution of a technology and a major technological leap.
- B. The effect of changes in treatment protocols – changes in clinical guidelines, duration of treatment, dosage and combinations with other technologies. Such changes have a direct impact on the extent and overall cost of the HSB.
- C. The interactions between registration and inclusion in the HSB.
- D. Budgetary uncertainty – disrupts the possibility for long term planning and multi-phase actions.
- E. How to respond to urgent situations, considering the cyclic nature of the process.
- F. The extent of public involvement in the process - how to make the public a participant and to what extent (transparency vs. undue pressure).

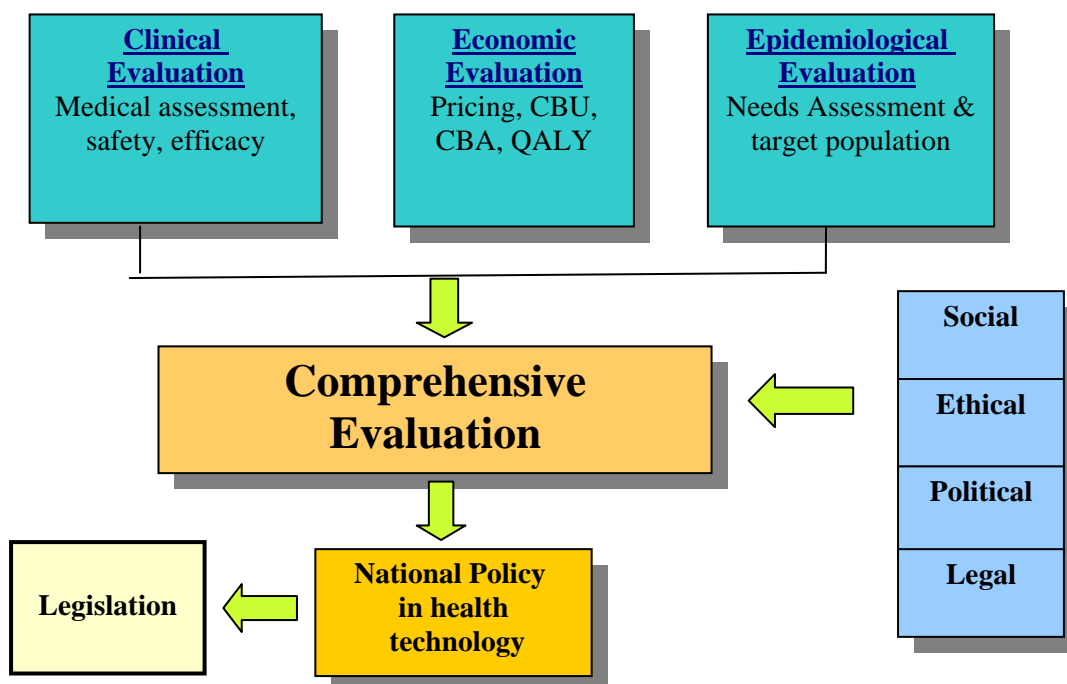
Summary

As learned by the experience of other countries, we too have learned that setting priorities is a complex process that involves making painful decisions. Moreover, the decisions made should be socially accepted by both the public affected by them and health professionals who have to implement them.

The updating process of the HSB has been widely accepted by the political system, judicial system and the public in Israel. Although we consider the process to be a practical and feasible mechanism, we constantly strive to further improve and make the process more efficient.

Every day emerges a new dilemma, challenging us to find new and innovative ways to solve it

Figure 1: An adapted model of updating new technologies



Appendix A: Guidelines for the submission of a request to include a medical technology in the "Health Services Basket" (HSB)

1. **General instructions for submission of a request to include a medical technology in the health services basket:**
 - 1.1 A request to include a medical technology in the HSB will include a comprehensive data file which will be submitted to the Medical Technology Administration (MTA), according to the guidelines detailed herewith.
 - 1.2 Medical technology refers to medical technologies, medical devices, apparatus, medical procedures and the organization of frameworks
 - 1.3 One data file will be submitted for all dosage forms, for all strengths and approved indications of the medical technology.
 - 1.4 All data and references will be in Hebrew and/or English. Official documents should be submitted in their original language. If the submission is only in English, a Hebrew translation of the summaries of parts II and III must be attached (see section 3.1.6 and 3.1.7).
 - 1.5 Submission of the file will be also on electronic media.
 - 1.6 Inclusion of a medical technology in the health services basket is done on the basis of a predefined budget, according to decisions made by the public committee for the update of the basket appointed by the Ministers of Health and Finance. The MTA will consider each application and after assessment will pass its recommendations to the appropriate authorities. Therefore, a complete and detailed request does not guarantee the requested medical technology to be considered by the appropriate authorities for inclusion in the health services basket or implicates the Ministry of Health in any possible way.
However, the process of decision making is based on the data submitted in the request and hence the great importance of the request's content.
 - 1.7 The data submitted will be processed by the MTA and presented to the public committee in a uniform format.
2. **Structure of the data file:**
 - 2.1 A request to include a medical technology in the national health services basket will be composed of three parts to be submitted according to section 3 of these guidelines:
Part I: Request forms and documents pertaining to details of the medical technology and a detailed summary of the data presented in parts II and III.
Part II: Clinical and epidemiological data.

Part III: Clinical-Economic evaluation.

- 2.2 The request will be submitted in a single binder separated by dividers.
- 2.3 On the back of the binder the name of the medical technology and the license holder's name, will be stated.

3. **Dossier elements:**

3.1 **Part A - General:**

- 3.1.1 Index
- 3.1.2 General description of the technology (Form 1).
- 3.1.3 One page summary of the disease's nature and the medical technology's relative benefits in comparison to the therapeutic alternatives that are included in the basket.
- 3.1.4 The technology's registration certificate (including full indications).
- 3.1.5 Technology monograph (if there is none - Full prescribing information (Physician leaflet)).
- 3.1.6 Detailed summary of the data presented in part II.
- 3.1.7 Detailed summary of the data presented in part III.
- 3.1.8 An affidavit of the medical technology's price in Israel (Form 2) - The medical technology's price in Israel is defined as the selling price for the Health Funds/Hospitals assuming the technology will be included in the basket.

3.2 **Part II – Clinical and Epidemiological data:**

3.2.1 **Clinical-Pharmacological profile:**

Briefly describe the general pharmacological profile of the medical technology's therapeutic class and the specific medical technology, according to the following points:

3.2.1.1 **The medical technology:**

-Recommended and commonly used treatment regimens with the technology, including expected length of treatment.

-If the medical technology is indicated for use in combination with other medical technologies, these combinations should be detailed.

- Summary of the adverse effects reported as part of the technology's post marketing surveillance (for pharmaceuticals – a summary of the last PSUR).
- Significant adverse effects, precautions / warnings and drug-drug interactions.
- Which changes have been made, if any, after receiving the marketing authorization (warnings, side effects, etc.)
- If the medical technology is being used in Israel under regulation 29 a(3), describe for which indications and how many patients are treated according to this approval.
- Detail other indications currently under research or any off label use of the medical technology, including all approved indications abroad (please state date of approval for each indication).

3.2.1.2 **The Therapeutic class:**

- Name of the therapeutic class and its classification according to standard classification systems.
- Major pharmacological action of medical technologies in this class.
- The rationale for using medical technologies of this class.

3.2.1.3 **Alternative treatment options:**

What are the major treatment options currently existing in Israel for the same indication. For each treatment option specify whether or not it is included in the basket.

For each alternative medicinal treatment option summarize according to the following points: Brief pharmacological profile; mechanism of action; rationale for use; efficacy and major side effects.

Please emphasize the aspects that differ significantly from the proposed medical technology.

It is recommended that the data presented will be in a tabular form.

3.2.1.4 Summarize briefly results from relevant clinical trials pertaining to the medical technology's efficacy for the relevant indication.
Preferably use comparative studies in which the proposed medical technology is compared to other treatment options used for the same indication (see explanation in paragraph 3.2.5).

3.2.1.5 Attach any official treatment guideline/protocol for the requested indication/s (in Israel and / or other countries) in which the proposed technology is part of. Highlight the relevant part regarding the proposed technology.

3.2.1.6 State how does the treatment with the proposed medical technology influence patient survival (percentage or in “months of living”)

3.2.1.7 State how does the treatment with the proposed medical technology influence the patient’s quality of life (if available list studies and data such as QALY)

3.2.1.8 Briefly summarize studies assessing the clinical outcomes of the treatment, such as indices of morbidity, mortality, quality of life, aspects of cost effectiveness and more.

3.2.1.9 **Expert report:**

3.2.1.9.1 An expert report by at least one physician specializing in the field the medical technology is indicated for, should be submitted.

3.2.1.9.2 The expert report must be based on all the data presented in the request and refer to the following points:

- Efficacy and importance of the medical technology in comparison to alternative treatments for the same indication.
- Personal experience with the medical technology.
- Definition of the medical technology's place in therapy (such as second/third line, specific patient groups to benefit the most from the treatment, etc.)

3.2.1.9.3 At the end of the report the following signed statement will appear:
“I am a physician, qualified to give this expert report on behalf of the requesting party. I give this expert report in support of a request to include this medical technology in the National Health Services list, according to the National Health Insurance Law, based on the entire file presented before me and my personal experience.

Herewith are details of my status and education:

I hereby declare that this is my name, that is my signature and the content of my expert report is true.”

3.2.1.9.4 Each expert report must be accompanied by a signed form of proper disclosure (See appendix B)

3.2.1.9.5 Expert reports that do not meet with the above mentioned criteria will not be taken under consideration.

3.2.2 **Pharmacoepidemiological data**

3.2.2.1 Summarize briefly the disease state to which the medical technology is indicated for (pathophysiology and clinical course) and the typical gradual treatment regimen.

3.2.2.2 The disease’s epidemiology:
- Prevalence: number of patients in Israel.
- Incidence: number of new patients each year in Israel.
Include, where available, incidence and prevalence data from other western world countries.

3.2.2.3 What is the market size (number of patients treated currently for the specific disease state) and its distribution for each of the treatment options detailed in section 3.2.1.3 (Use market surveys data, IMS, etc).

3.2.2.4 Cite the Israeli sales figures of the requested medical technology from the last three years.

- 3.2.2.5 By how much is the target population expected to increase within the next three years following inclusion of the proposed medical technology in the basket.
- 3.2.2.6 Is the requested medical technology included in a Health Fund's formulary in Israel (If so, in which Health Fund, date of inclusion in the formulary, rate of co-payment and type of insurance).
- 3.2.2.7 Is the requested medical technology included in a formulary of a public insurer in other countries (state name of country and rates of co-payment).

3.2.3 **The new treatment equilibrium:**

- 3.2.3.1 As part of the treatment regimen what is the requested place of the medical technology.
- 3.2.3.2 How many patients are expected to switch from their current treatment to the proposed medical technology (based on clinical and/or economic considerations) after inclusion of the proposed medical technology in the health basket.
- 3.2.3.3 Characteristics of the specific patient population which will benefit the most from receiving treatment with the proposed medical technology.
- 3.2.3.4 After inclusion of the proposed medical technology in the health basket what is expected to be the new market share for each treatment option (what percentage of the patients will be treated with each treatment option).
- 3.2.3.5 Is the market expected to grow after inclusion of the proposed medical technology in the health basket (will the number of treated patients increase)? If so, by how much.

3.2.4 Medical technologies that will bear no added cost to the basket according to the dossier submitter's assessment:

Attached to the full dossier will be a segment detailing the arguments as to why the inclusion of the proposed medical technology will bear no added cost to the health services basket. This part will be based on a comparison to therapeutic alternatives that are included in the basket.

In such a case, submission of a full dossier is necessary to ensure discussion of the requested medical technology as any other proposed technology, in case there will not be an agreement as to the technology not adding costs to the basket

3.2.5. Supporting clinical information:

- 3.2.5.1 Attach a printout of the previous year's abstracts.
- 3.2.5.2 For each clinical trial cited attach the original paper / source. Moreover for each trial summarize the following data elements:
 - 3.2.5.2.1 Name of trial.
 - 3.2.5.2.2 Location and trial date.
 - 3.2.5.2.3 Publication citation/s.
 - 3.2.5.2.4 Trial design, randomization and blinding procedures.
 - 3.2.5.2.5 Inclusion and exclusion criteria.
 - 3.2.5.2.6 Treatments to which the proposed medical technology was compared (including placebo).
 - 3.2.5.2.7 Treatment and dosage regimens
 - 3.2.5.2.8 Sample characteristics: demographics, sample size, disease severity and comorbidities.
 - 3.2.5.2.9 Patient follow-up procedures: if intention to treat, were drop-outs followed ?
 - 3.2.5.2.10 Clinical and other outcomes measured and their statistical significance.
 - 3.2.5.2.11 Compliance behavior.
 - 3.2.5.2.12 Concordance of the achieved outcomes in the trial's sample and the actual expected outcomes in the target population (considering differences of treatment protocol, treatment populations, comorbidities, compliance, follow-up, etc.). If such a difference exists, propose a model to link the trial's results with the expected outcomes in Israel while detailing the justification to the model's assumptions.
- 3.2.5.3 If meta analyses have been undertaken, these should be summarized with particular emphasis on the inclusion criteria for studies analyzed.
Justify the relevance of the analysis to the target population.

- 3.2.5.4 Where a retrospective study has been undertaken (utilizing pharmacy and medical claims databases) the study should be summarized and should include, in addition to the above information, the research question or hypothesis tested, rationale for the study design, choice of data source, techniques used to assess data quality, rationale for chosen statistical or econometric procedure and techniques used to avoid issues such as selection bias.

3.3 **Part III: Economic evaluation**

- 3.3.1 An economic evaluation of the proposed medical technology must be submitted (See instructions in Appendix A: Instructions for performing an economic assessment).
- 3.3.2 An economic evaluation conducted abroad should be adapted to Israeli settings. In such cases the request will include both evaluations.
- 3.3.3 The economic evaluation will be performed according to one of the accepted models, taking into account the following elements:
- 3.3.3.1 Estimated target population.
 - 3.3.3.2 Savings in healthcare resources (hospitalization, physician visits, etc.).
 - 3.3.3.3 Savings in medical technologies.
 - 3.3.3.4 Comparison to cost of alternative registered treatments in Israel.
 - 3.3.3.5 Cost of treatment.

Form 1

General description of the medical technology

Name of the technology: _____

Registered dosage forms in Israel (including dosage forms, strength/concentration, package type and quantity/size and registration number):

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____

Active ingredients (Generic names) and their quantity in dosing units:

1. _____
2. _____
3. _____
4. _____

Registered indications in Israel (including date of approval of each indication):

1. _____
2. _____
3. _____

Pharmacological classification of the technology:

1. Name of the technology's pharmacological class:

2. Known or assumed mechanism of action of the technology:

Other countries in which the technology is registered and the registered indications in each country (if different from the registered name in Israel):

Is the technology indicated for use in combination with any other technology ?

General:

Name of license holder:

License holder's address (in Israel and abroad):

Affidavit:

To my knowledge and professional responsibility, I, the undersigned, declare herewith that all the data submitted in this request are correct.

Name of the application
submitter

Stamp and signature

Date

Form 2

Affidavit of the technology's price

ISRAEL

Dosage forms					
Strength					
Package type and quantity					
Price per package (for institutions)*					
Number of estimated patients					

*Institutional Price – the selling price to the Health Funds / Hospitals if the technology will be included in the basket

Global:

Current institutional price in The Netherlands, France, Belgium, Germany, Great Britain, Spain, Portugal, Hungary and Poland (Fill the form separately for each country):

Country					
Dosage forms					
Strength					
Package type and quantity					
Price per package (for institutions)*					
Number of estimated patients					

 Name of the license holder
 or a corporate manager who
 is the license holder

 Stamp and signature of the license
 holder or the corporate manager who
 is the license holder

 Date

Appendix A: Instructions for performing an economic assessment

1. Assessment clinical outcomes:

- 1.1 Define the clinical outcomes (including indices of quality of life) indicative of a successful treatment. Intermediate or final outcomes may be used. If intermediate outcomes are selected then the analysis should be supported by evidence to show how these outcomes are linked quantitatively to final outcomes.
- 1.2 What are the desired values for the outcomes mentioned above, which define a treatment as successful.
- 1.3 What is the number of patients in Israel that achieve the wanted clinical outcome with the current treatment options. (Defined as the sum of the product of the percentage of patients achieving the wanted outcome in each of the existing treatment options and the number of patients treated with each treatment option, in a given year).
- 1.4 What is the expected impact of the proposed medical technology on the disease's treatment outcomes (the value received in section 3.3.4.1.3 after taking into consideration the new treatment equilibrium).

2. Assessment of the cost to health services providers:

- 2.1 Identify the resources used for the proposed indication for each of the treatment options currently existing (including the treatment itself, resources used to support therapy and resources used to treat side effects and treatment failures).
- 2.2 Estimate the cost to the Health Funds / Hospitals for each unit of the resources mentioned in the previous section. As to the cost of the proposed medical technology itself, a signed affidavit of the medical technology's price in Israel must be submitted (Form 2). The medical technology's price in Israel is defined as the maximal selling price for the Health Funds / Hospital if the medical technology will be included in the basket.
- 2.3 Assess the overall annual cost of treatment of the proposed indication to the Health Funds / Hospitals (A model based on cost of resources and clinical outcomes mentioned before, may be used).
It is preferable to use the Ministry of Health's ambulatory services' price list when pricing a non-medicinal treatment of the disease.

- 2.4 Assess the cost of resources which will be used to treat the disease-state, in the first three years following the inclusion of the proposed medical technology in the health basket. In this assessment consider the size of the market and the expected new market shares.
- 2.5 What is the net impact of inclusion of the proposed medical technology in the health basket on the total cost of treating the disease-state to the Health Funds / Hospitals.

3. Cost effectiveness evaluation

A comprehensive evaluation of the expected benefit to the treated population, after inclusion of the proposed medical technology in the health basket, will be submitted which will include the following elements:

- 3.1 Overall assessment of the impact of the proposed medical technology on the cost of treatment of the target population in the first three years following the inclusion of the proposed medical technology in the health basket.
- 3.2 Overall assessment of the proposed medical technology's impact on the treatment's outcomes.
- 3.3 Impact of the uncertainty of the different data on the strength of the above assessment (sensitivity analysis of the evaluation)

4. Supporting pharmacoeconomic information:

- 4.1 For each pharmacoeconomic study/trial summarize the following data elements:
 - 4.1.1 Name of trial, date and location, length of trial.
 - 4.1.2 Publication citation/s.
 - 4.1.3 Research question.
 - 4.1.4 Type of economic study.
 - 4.1.5 Study perspective.
 - 4.1.6 Study design.
 - 4.1.7 The treatment to which the medical technology was compared and the reasons it was chosen.
 - 4.1.8 Inclusion and exclusion criteria.
 - 4.1.9 Sample characteristics: demographics, sample size, disease severity and comorbidities.
 - 4.1.10 Treatment protocol.
 - 4.1.11 Resource utilization and unit costs.
 - 4.1.12 Outcomes selected.
 - 4.1.13 Principal findings and their statistical significance.
 - 4.1.14 Relevance to the treated population in Israel.

- 4.2 Cite studies which analyze the economic impact of the use of the proposed medical technology that are relevant to the information requirements of the public committee.

Please pay attention to the fact that most economic studies that appear in the scientific literature analyze the economic impact in terms of incidence. These studies compare the costs of the different treatment options in a single patient from the stage of diagnosis throughout the course of the disease. Since the public committee deals with allocating an annual budget to the Health Funds, the Israeli guidelines request information which will assist the committee in assessing the impact of the proposed medical technology on the annual cost of treatment to the Health Funds, to treat all the patients in Israel in a defined period of three years following inclusion of the proposed medical technology in the health basket. Therefore, it is of great importance that the economic data and the supporting pharmacoeconomic studies submitted to the committee, examine the impact of inclusion of the proposed medical technology in the health basket in terms of prevalence and not in terms of incidence.

- 4.3 As supporting data, one may use economic evaluations based on clinical trials. In such cases, it must be examined whether the extrapolation or the model are relevant to the Israeli settings (patient characteristics' wise: comorbidities, compliance, type and quantity of resources used, cost data).

- 4.4 When citing an economic evaluation based on an epidemiological study or retrospective data (and not on a prospective clinical trial), detail carefully the study's design, different factors which might influence the study's results (confounding variables) and the techniques used to overcome them, the methodology used when the economic evaluation or the model were performed, statistical analysis of the results, and the relevance of the results to the local settings.

Appendix B:
Recommendation for the health services basket – Proper disclosure form

Date: _____

Since I intend to give my professional opinion regarding the medical technology _____ manufactured by _____, to be submitted to the public committee responsible for the update of the Health Services Basket, Advising the Ministers of Health and Finance regarding inclusion of new technologies in the health services basket, according to the National Insurance Health Law, I declare as follows:

1. I hereby confirm that I do not work for the company _____, I am not an advisor to it, I do not perform trials for it or commissioned by it, for a payment, whether directly or indirectly, I do not hold any position or job in its institutions, or connected to it in any other way which will prevent me from giving my professional opinion in an objective fashion and/or in a way that might cause a conflict of interest. I am not connected to this company in any other way and have not been in contact with it by one or more of the above mentioned affiliations, even in the past, whether for the proposed medical technology or for any other medical technology.

Confirm

Do not confirm

2. I hereby confirm that I do not know of any possible competition between any body or bodies with which I am connected in one or more of the manners detailed above, regarding the medical technology or the issue of its inclusion in the health services basket, which will prevent me from giving my professional opinion, in a way that might cause a conflict of interest.

Confirm

Do not confirm

3. I hereby declare that I am connected in one or more of the manners detailed in section 1, detailed herewith:

Name: _____

Signature: _____