Israel Compliance Issues Update

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Agenda

• The setting: Israel and its pharmaceutical market
  – Overview
  – Registration of pharmaceuticals, pricing and reimbursement
  – Health Insurance

• Pharmaceutical compliance issues in Israel
  – Regulatory Background
  – Current Status of Pharmaceutical Compliance
The Israeli Economy and the Israeli Pharmaceutical Market
Israel – Basic Facts

- Area: 22,072 sq.km
- Population: 7.9 million
- GDP (US$ bn PPP): $204.4
- GDP per capita (US$): $28,390
- Growth in GDP: 0.7%
- Inflation rate: 3.9%
- Unemployment rate: 7.5%
- Babies born per year: 161,000

Source: Central Bureau of Statistics 2009/12
Innovation - 1st in Medical; 4th in Biopharma

Source: USPTO
Israel – Health Care Market

- 23 General Hospitals
- 11,500 Nurses
- 1,300 pharmacies (550 institutional)
- Total health expenditure -- $15 Billion
- Israeli pharma market US$ 1.2 to 1.5 billion
  - 60% ethical products, 40% generics (by value)
  - Approx. 63% products imported
Israel – Hospitals

• Ownership
  – The MoH owns and operates about ½ of the nation’s hospital beds, in addition to its regulatory, planning roles.
  – Clalit, the largest health fund, operates another third of the beds.
  – The remainder are operated by means of a mix of not-for-profit and for-profit organizations.

• Hospital revenues are derived primarily from the sale of services, with 80% coming from sale of services to health plans.

• Reimbursement of public hospitals takes the form of fee-for-service payments, per diem fees and case payments, and is subject to a revenues cap.
Israel -- Physicians

- 25,542 doctors (2010): 3.36 doctors/1,000 inhabitants.
- Approx 50% of all registered physicians are specialists.

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<thead>
<tr>
<th>Medical Specialty</th>
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<td>Cardiology</td>
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<td>Endocrinology</td>
<td>143</td>
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Israel - Research Activity

• 30 institutions
  – 20 university hospitals under 5 universities
  – Weizmann institute
  – 4 HMOs
  – other
• 203 medical research & development companies
  – International Pharma affiliates
  – Israeli multinational pharma (e.g., Teva)
  – Biotechnology companies
  – CROs
  – More

1. Dun & Bradstreet, 2009
Israel - Clinical Trials

- World class health system
- Professional physicians and investigators
- Renowned institutions
- High patient compliance and retention rate
- Heterogeneous population
- Geographic proximity
- Good research foundation
- ICH GCP mandatory
- FDA recognition

clinicaltrials.gov
Rotmensch, 4th ACRP annual meeting, Israel 2008
Pharma Israel clinical trials convention, Israel 2006
Israel – A Target for Medical Tourism

• Israel emerging as popular destination for medical tourists:
  ➢ 2006 - 15,000 foreigners visited for treatment ($40 million revenue)
  ➢ 2010 – 30,000 foreigners visited for treatment

• Various reasons:
  ➢ Some come from nations where certain procedures are not available.
  ➢ Others come because they can receive quality health care at a fraction of the cost it would be at home, for both surgeries and in-vitro fertilization procedures.
  ➢ Other medical tourists come to Israel to visit the Dead Sea, a world-famous therapeutic resort.

Source: Wikipedia: Health care in Israel
Israel – High Expenditure on Health Care

Source: OECD Health Data 2009, November 2009 and Israel central bureau of statistic
Registration and Pricing of Pharmaceuticals in Israel
The Israeli Regulatory Environment

• Basic Registration Procedure: only if it is registered and marketed in a country which is recognized by Israeli MoH (U.S., original members of E.U, Australia, New Zealand, Canada, Switzerland, Japan, few others).

• MoH maintains “European attitude” towards safety, quality, efficacy.

• Registration is CPP dependent. However, submission is possible based on CHMP positive opinion prior to CPP availability.

• Named-patient regulation enables importation and sales of non-approved drugs.
Regulatory/Registration Process

- File Preparation: -18 months
- Submission: -15 months
- Approval: -2 months
- First Batch: -1 month

• Review Process May be Significantly Accelerated

Source: Ministry of Health
Israel – Pharmaceutical Pricing

- Regulated by the MoH price controller
- The “Gazette Price” or Maximum Price to the pharmacist is calculated based on the average product’s price in certain EU reference prices.
- Maximum for inclusion in a national list of reimbursed products equals the Gazette Price less discount of 6-8% (amount of discount may vary from year to year).
The MOH Drug Basket

• Priority Setting Process for Inclusion of new technologies in national list of reimbursed drugs (the “Basket”)

• Annual formal priority-setting process:
  – Gov’t determines annually size of budget available to fund new technologies.
  – MOH solicits recommendations for the health plans, pharmaceutical companies, Israel Medical Association, patient organizations and other groups for new technologies to be given priority for inclusion in the benefits package.
  – MOH undertakes a cost-benefit analysis.
  – Public committee (composed of health plan representatives, the MoH and the Ministry of Finance, Israel Medical Association, experts in health economics and health policy, and public figures) recommends which new technologies should be adopted
  – The public committee’s recommendations are not legally binding, but to date its recommendations have been fully adopted by the MOH.

➢ 2010 budget of 350M NIS was allocated to 78 new medical technologies which had been selected out of +500 submissions
Health Insurance in Israel
Israel – National Health Insurance

- **1995 National Health Insurance Law**: membership in one of the four existing HMOs compulsory for all Israeli citizens.
- **Uniform benefits package for all citizens** - which each of the HMOs required to fund for its members. Additionally, certain services under the direct administration of MOH.
- **System of public funding** for health care services by means of a progressive health tax and general tax revenue.
- **Free choice among the 4 competing HMOs.**

The Health Funds

• The largest health plan, Clalit, has a market share of 52%. It provides community-based services, primarily via salaried physicians working in clinics that it owns and operates.
• The next largest plan, Maccabi, has a market share of 25% and provides care primarily through a network of independent physicians
• 77% of the population covered by additional complementary insurance
Innovation from a patient’s perspective

- Online lab results
- Free SMS reminder service for medication
- Free Online video chat with a pediatrician during nights & holidays
Pharmaceutical Companies Presence in Israel

• All major pharma companies are active in Israel: many operating their own Israeli affiliates; some through distributors.

• Of the top 25 pharma companies, only 4 companies are not active in Israel – all of which are Japanese.

Source: U.S. Commercial Service www.buyusea.gov/healthcare/israelwebinar.html
Pharma Israel - The organization of R&D based Pharmaceutical companies

- Roche
- Actelion
- Lilly
- GlaxoSmithKline
- Janssen
- Abbott
- Merck
- Pfizer
- Novartis
- Genzyme Israel
- MSD
- Lundbeck
- Novo Nordisk
- Bayer HealthCare
- Sanofi Aventis
- AstraZeneca

Pharma Israel
The Association of the research based pharmaceutical companies
Gov’t Role in Pharma Sector

• MOH approves pharma products for sale, establishes NHI formulary, sets price ceilings, licenses pharmacists.

• Strong MOH capabilities in areas of technology assessment, prioritization of new technologies, HMO regulation, quality monitoring for community-based care, national strategic plans

• Ministry of Finance has multiple points of influence over health care, which it uses to try to contain health care spending, to improve services and to increase efficiency of the system.

Source: Wikipedia: Health care in Israel
Pharmaceutical compliance issues in Israel
General Anti-Bribery Initiatives in Israel

- Steps Taken to Implement and Enforce the OECD Convention on Combating Corruption in International Business:
  - 2008 and 2010 Amendments to the Penal Law, 1977
  - Ratification of OECD Convention deposited with OECD Secretary General in 2009.
  - 2009-11 Various amendments to tax legislation, including non-deductibility of any payments made “in violation of any law.”

Source: OECD publication, February 20, 2011
But Declining Perception of “Transparency”:

- Decline to 36th place in 2011 from 30th in 2010 in TI’s CPI; lowest Israeli ranking since included in index.
- Israel ranked 25/34 OECD member states (ahead of Turkey, Italy and Greece)

Source: Globes business newspaper, December 1, 2011
Codifying the relationships in Israel

- Sec 28 of the Pharmacists ordinance prohibits advertisement of prescription medicine
- The Joint Ethical Convention 2004 Signed by Industry, IMA, HMO's
- Transparency of Contributions Act
- IMA code regulating physicians activities + committee
The Joint Ethical Convention of the Israel Medical Association and Pharmaceutical Companies Operating in Israel, October 2004

Signed in presence of MOH and Chairman of the Knesset Employment, Welfare & Health Committee

One document, two codes:

- Code of Ethics of Israel Medical Association regarding relations between physicians and commercial companies
- Marketing Code of Ethics of Pharmaceutical Companies Operating in Israel
Marketing Code of Pharma Companies:

- Main rules address:
  - Standards of promotion
  - Medical representatives
  - Symposia, congresses and other means of verbal communication
  - Hospitality and promotional items
  - Printed promotional material (including internet)
  - Samples
  - Complaint procedure
Standards of Promotion: accurate and conform to legal requirements, high ethical stds and high professional stds.

Education: disclosure of sponsorship; not conditioned on promotional obligations; reasonable honoraria and out-of-pocket expenses

Travel abroad and participation in seminars: to be facilitated through research fund or ass’n or medical institution permitted – not to HCP

Hospitality: reasonable amount

Samples: not to be distributed in commercial quantities
Developments since 2004

- Proposed 2012 amendments to Joint Convention:
  - **Gifts:** Medical Utility Items – permitted, no “tchotchkes” (pens, pad, other nominal gifts)
  - **Meetings/Hospitality:** No luxurious (and spa-like) locations; no entertainment (or the sponsorship of such)
  - **Consulting Agreements:** Written agreements, obligation on HCPs to report, if required
But ... a critical review:

- Standards of Promotion: vague
- Education: no CME requirements in Israel
- Hospitality: still vague
- Contributions: Statement only “to be give only for professional reasons” but no prohibition if fails to meet this standard.
- Consulting Agreements: HCP’s reporting obligation unclear
- Samples: No across the board rules – Per company (Pfizer – no samples, AZ – very limited - clustered)

- No clear indication when Covention to be amended.
- Out-dated convention; no real enforcement
Developments since 2004

- Israel’s Current “Sunshine Act”: The Transparency in Contributions Act (2009)
  - Donors and donees each to report to MOH by May 1, donations in prior year exceeding 2,500 NIS/year in aggregate (approx US$700): breakdown of every contribution (type, amount, purpose).
  - First report published May 2010 (for ‘09) – but no figures required.
2011 Distribution of Donations by Donees (donations made by members of Pharma Israel only)

(in 000’s NIS. Total = 21.2M NIS (~US$6M))
2011 Pharma Israel Donations by Purpose of the Donation

- **Support for overseas training and education**: 293,000 NIS
- **Other**: 37,000 NIS
- **Support for local institutional training**: 7,259,000 NIS
- **Participation in purchase of medical equipment**: 5,097,000 NIS
- **Participation in in-country training**: 20,000 NIS
- **Renovation/building financing**: 8,498,000 NIS

*(in 000’s NIS)*

Source: Pharma Israel
Donations in Category “Other”

- General ass'n activity: 47%
- Support for medical projects: 13%
- Medical education: 12%
- Medical training: 6%
- Research: 4%
- Patient welfare: 3%
- Social projects: 2%
- Medical aid: 11%
But ... a critical review:

- **Definition of Contribution:** vague—some companies received legal opinion that nothing required to be reported

- **HCP Reporting:** HCP’s paid for service rendered; unlikely that any HCP will have any reporting obligation

- **Sanctions:** none in the law

- **Transparency the aim; but question whether really achieved**