Reprinted from
PHARMACEUTICAL ENGINEERING®
The Official Magazine of ISPE
May/June 2006, Vol. 26 No. 3

Country *Profile*

A look at the Pharmaceutical Industry in

TURKEY

Produced in collaboration with ISPE Turkey

ENGINEERING PHARMACEUTICAL INNOVATION

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Dear ISPE Members,

On behalf of ISPE Turkey Affiliate, it is a pleasure for me to have the opportunity to make you more familiar with our country, our pharmaceutical industry, and our rather young Affiliate.

The roots of the Turkish pharmaceutical industry date back to the beginning of the 19th century. Today, the pharmaceutical industry represents nearly 300 companies in Turkey, of which 135 are major, and employment is approaching the 25,000 mark. It is in this context that we have launched the new ISPE Turkey Affiliate. One of the Affiliate's primary objectives is to contribute to the development of a common platform representing various manufacturers and suppliers of the industry, including academia, public authorities, and government agencies. The aim of such a platform is to foster progress within the industry. This cooperation among parties is to be supported by three to four educational seminars per year to promote dissemination of current knowledge and best practices.

In addition to these activities, we also are planning with the overall support of ISPE at large to promote the concept of the "professional pharmaceutical engineer." This goal shall be pursued in cooperation with Educational Foundations and as a response to the current high demand for training for pharmaceutical technicians by both industry and academia.

The enthusiastic support we received from the pharmaceutical industry at the inaugural seminar of our Affiliate last December reinforced our confidence and strength in the pursuit of the established milestones.

I hope this profile will fulfil its mission of giving a good picture of the Turkish pharmaceutical industry.

Sincerely,

Ünsal Hekiman

Chairman
ISPE Turkey Affiliate

This feature in *Pharmaceutical Engineering* is designed so that you can tear it out, three hole drill (if desired), and keep it with other Country Profiles as they are published.

Chronology of Turkey's Pharmaceutical Industry and its Outlook for the Future

by Selim Seyhan, Manager of R&D and Training, PharmaVision

Highlights

Turkey is considered to be one of the 35 pharmaceutical producing countries in the world. With preparations being offered as early as the beginning of the 19th century, large scale manufacturing started before the Republic (1923). Starting in 1915, mainly in drug stores and laboratories, around 30 products, ampoules, drops, syrups etc. were produced. After the establishment of the Turkish Republic, between 1928 and 1950, manufacturing was conducted in laboratories and small plants. After the Second World War, manufacturing capacity was increased with the establishment of local and foreign invested plants commencing in 1952. From 1984 onward, investments of foreign capital companies have increased. Especially after 1990, many foreign capital firms have entered the Turkish pharmaceuticals market. According to the last available data, about 300 entities are operating in Turkey, including 85 Drug Product (DP) plants and 11 API plants.

- Two of the plants are owned by the state.
- Eight foreign capital firms have their manufacturing facilities in Turkey.
- 27 foreign capital firms are supplying their products by imports or using subcontractors' manufacturing facilities in Turkey.
- There are 97 local capital firms.

Year	Raw Material (tons)	Finished Product (million boxes)
1998	7076	923
1999	5552	1005
2000	4980	1094
2001	4382	952
2002	3909	969
2003	circa 3900	circa 1129
2004	circa 3000	circa 1321
2005	circa 3000	circa 1366

Table A. Pharmaceutical production in Turkey.

After the official application of the GMPs in 1984, the Turkish Pharmaceutical Industry, making necessary investments, reached a technological level which can almost be compared to EU countries except in biotechnology and a few state-of-the-art technologies.

Consumption of Finished Product

Latest figure for the Turkish pharmaceutical market size is around US $6.6 billion (close to

Professions	Number Employed
Administrative staff	3,969
Workers	3,366
Skilled workers	2,338
Other engineers	1,600
Economists	1,255
Biologists	1,113
Chemical engineers	910
Chemists	853
Technicians	615
Pharmacists	514
Doctors	374
Laboratory assistants	212
Other personnel with university degrees	4,695
Total	**21,814**

Table B. Pharmaceutical employment in Turkey - 2005.

Continued on page 78.

General Information on Turkey

With a yearly growth rate of 9.9 %, currently one of the highest in the world, a market of 70 million people, a well established pharmaceutical manufacturing base and EU accession talks underway, the establishment of an ISPE Affiliate in Turkey is more relevant than ever before.

Investments by foreign capital companies have steadily increased in the past 20 years with this trend expected to continue, taking into account the country's proximity to European markets and its qualified and relatively inexpensive workforce. According to data provided by the Ministry of Health, there are 300 companies in the Turkish pharmaceutical market, of which 52 are foreign owned. 85 companies have their own manufacturing facilities, 11 are API producers. The rest of the companies are supplying their products by means of imports or by using subcontractors' production facilities in Turkey. A general overview of the scope of the Turkish pharmaceutical industry is further detailed in later sections of this profile.

With an area of nearly 800,000 square kilometres spread between Europe and Asia, the country's strategic geographical location between East and West is further emphasized by its cultural and political closeness to several governments in the region with conflicting political views.

Chronology of Turkey's Pharmaceutical Industry...

Continued from page 77.

Year	Exports (US$ million)	Imports (US$ million)	Export/Import Ratio (%)
1998	129	1181	10.9
1999	128	1337	9.6
2000	140	1511	9.3
2001	149	1534	9.7
2002	157	1716	9.2
2003	246	2419	10.2
2004	248	2710	9.2
2005	282	2850	9.9

Table C. Export/import ratio in the pharmaceutical industry.

half of it accounted by imports), making it the 12th largest drug market in the world.

Projections for 2023

Market worth is estimated to reach US $25 billion; US $100 per capita annual spending on drugs; US $800 million export; 55% import share in the market according to available recent data from various sources.

Statistical Data[1] about the Industry

In this section, you will find information, statistics, and other relevant data and graphics giving an accurate picture of the Turkish pharmaceutical industry.

Year	Total: Manufacturer Prices (US$ billion)	Of which, import (US$ billion)
2005	6.6	circa 3
2023 (projected)	circa 25	circa 12

Table D. Size of the Turkish pharmaceutical market (Source: Pharmaceutical Manufacturer's Association of Turkey).

Consumption

On a comparison based on Year 2004 figures, it can be concluded that per capita, pharmaceuticals consumption in Turkey (US $92) is quite lower than EU and other developed countries. A graphical comparison with several countries is given in Figure 1.

In treatment groups, according to 2005 figures, antibiotics are leading with a 17.8% consumption rate, anti-rheumotismals are second with a 12.4% consumption rate, followed by pain killers, cold treatment pharmaceuticals, and vitamins. The complete breakdown is illustrated in Table E.

Treatment Pharmaceuticals	Market Share (%)
Antibiotics	17.8
Pain-killers	9.5
Anti-rheumotismals	12.4
Cold and cough treatment pharmaceuticals	8.5
Vitamins, minerals and anti-anaemic pharmaceuticals	6.1
Skin diseases pharmaceuticals	4.9
Digestive system pharmaceuticals	5.2
Cardiovascular diseases pharmaceuticals	7.3
Hormones	4.0
Ear, nose, throat, and ophthalmic preparations	4.3
Nervous System pharmaceuticals	3.4
Diabetes pharmaceuticals	1.4
Others	15.2

Table E. Market share by pharmaceutical product category - 2005.

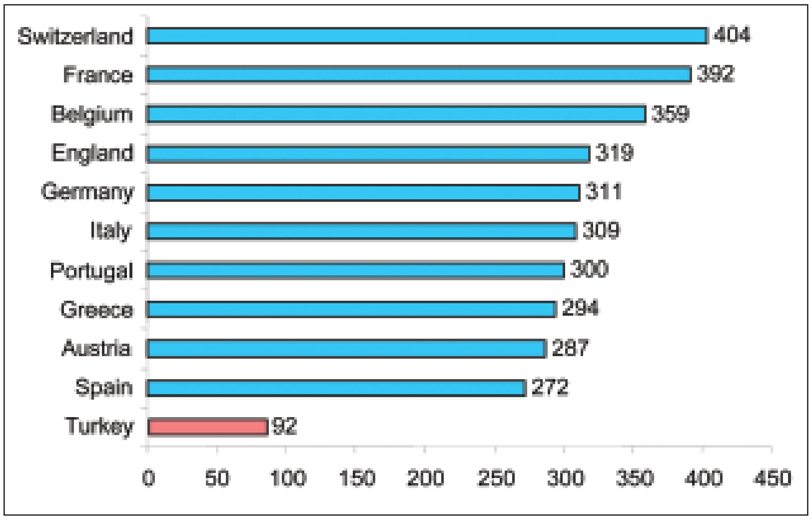

Figure 1. Per capita consumption rate in US$ of pharmaceuticals according to treatment groups - 2003 / data for Turkey is 2005.

Country	US$ million
Ireland	12.945
Switzerland	11.073
France	6.674
England	5.939
Sweden	4.373
Denmark	3.511
Germany	2.995
Netherlands	1.356
Austria	63
Belgium	-700
Norway	-710
Finland	-733
Turkey	**-1.019**
Italy	-1.157
Portugal	-1.306
Greece	-1.534
Spain	-3.007

Table F. Trade balances in finished goods - 2003.

Chronology of Turkey's Pharmaceutical Industry...

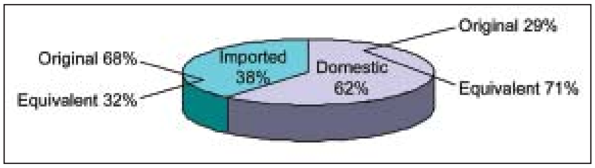

Figure 2. Market pharmaceutical distribution in terms of sales forms - 2005.

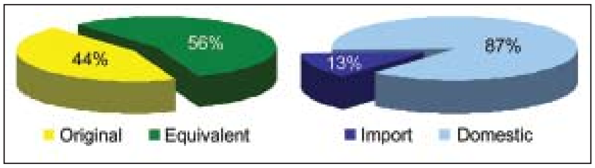

Figure 3. Original/equivalent and import/domestic distributions (packs) in pharmaceutical market - 2005.

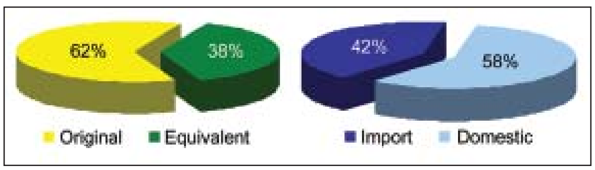

Figure 4. Sale amount ratios for original/equivalent and import/domestic - 2005.

The information in Figure 2 represents the market distribution in terms of local manufacture vs. imports, further divided into original preparations against generics.

Foreign Trade/Investments

The Turkish pharmaceutical industry, with the quality, efficiency, and reliability of its products has reached a level where it can compete with many countries. As a matter of fact, the industry performed exports to more than 50 countries including Germany, US, Austria, Belgium, Finland, Netherlands, UK, Switzerland, Italy, and Japan.

On the other hand, the industry faces certain obstacles. To compete more successfully in foreign markets, The Turkish pharmaceutical industry is increasing both its technical and marketing investments on a continuous basis. The foreign trade volumes are on the rise as shown in Figures 5 and 6.

One of the Affiliate's missions will be to increase the cooperation between the industry and the authorities to reverse this trend. With a well educated workforce and relatively cheap manufacturing costs, the stumbling block appears to be inadequate investments.

It is estimated that in order to closely align the technological developments in the world and the evolving GMP rules, the Turkish pharmaceutical industry must invest at an average rate of $100 million per year. The graph below indicates that the industry is steadily approaching this value.

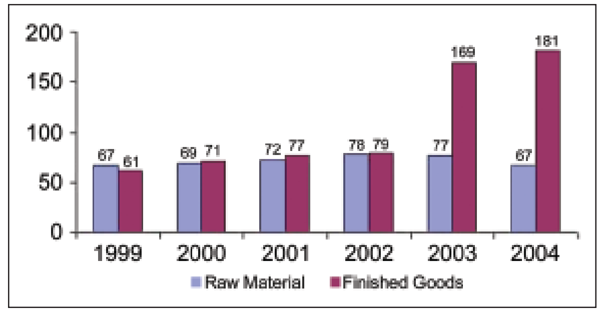

Figure 5. Exports in millions US dollars.

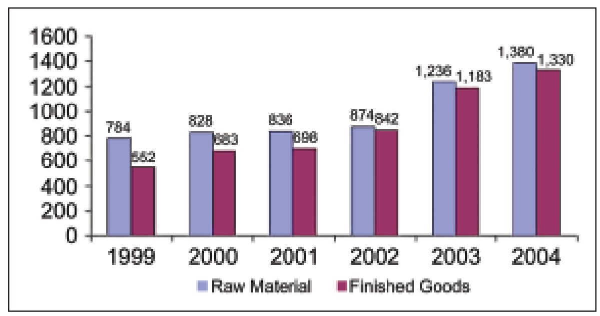

Figure 6. Imports in millions US dollars.

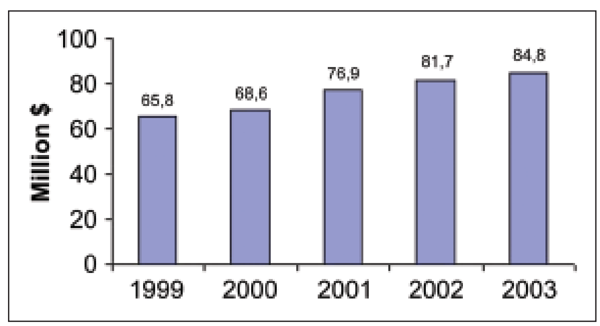

Figure 7. Turkey's investment growth rate in the pharmaceutical industry.

Investments in the Turkish Pharmaceutical Industry

With already planned measures showing their effects in the coming years, the industry is confident of surpassing its goals.

[1] Sources: European Federation of Pharmaceutical Industries and Associations (EFPIA), Pharmaceutical Manufacturers' Association (IEIS), The Scientific and Techonological Research Council of Turkey (TÜBITAK), and various company reports.

Case Studies

by Selim Seyhan, Manager of R&D and Training, PharmaVision,
Nuran Varolan, Technical Director, Pfizer Istanbul Site, and Suat Kumser, Aseptic Operations, Liquid, and Ointment Area Production Manager, Pfizer Istanbul Site

In this section, two case studies will be presented of companies demonstrating the level of manufacturing understanding reached in Turkey. PharmaVision is a pure contract manufacturing entity in Istanbul, and Pfizer Istanbul is a well established manufacturing site of the global Pfizer organization also in Istanbul. Many other leading Turkish manufacturing companies are also competing successfully on the international level.

PharmaVision

A Successful Management Buyout Case

PharmaVision, a leading Contract Manufacturing Organization (CMO) in Turkey, has a long history in the country, its roots going back to Türk-Hoechst Sanayi ve Tic. A.S, the Turkish subsidiary of the German Hoechst AG, was established in 1954 as one of the first foreign investments in our country. Through various mergers at the headquarter level over the years, the site became part of Hoechst Marion Roussel followed by Aventis, this transformation culminating in a management buyout in December 2002 with the creation of PharmaVision.

Over 50 years on its 51-acre manufacturing site in the Topkapi region of Istanbul, the company has witnessed various GMP upgrading in line with ever increasing regulatory and customer demands. A 12-year long multi-stage remodelling project commencing in 1987 has resulted in a technologically advanced factory with its computer supported, closed system, and uninterrupted manufacturing lines. Adapting to new technical advancements, further investments are in progress in an intensive manner.

Located on 51,000 m^2 campus, PharmaVision aspires to become a preferred partner in contract manufacturing to the pharmaceutical industry. The company's vision is in complete toll manufacturing partnership without any own licensing. Maintaining and continuously improving its high Good Manufacturing Practice (GMP) standard is attained by adhering to strict, effective, and updated Standard Operating Procedures (SOPs) as well as quality standards by continuously investing in its facility and equipment and by recruiting, properly training, and retaining top talent in the country. In line with current regulatory trends, and in addition to general non-betalactam manufacturing encompassing all galenical processing except lyophilization, PharmaVision has also separate production facilities for cephalosporin (sterile powder), penicillin (tablets, oral powder), and enzyme products (oral form).

The quality and compliance level reached through these modifications is further supplemented by continuous education and training of the staff, integration of modern quality management systems encompassing EHS, and risk assessment procedures. Such continuous efforts and a constant benchmarking of industry standards are all aimed at the mission of becoming the "preferred toll manufacturing business partner" not only on a national level, but a global one as well. In this roadmap, PharmaVision has collected several certificates, such as ISO 14001, OHSAS 18001, TS 13001 (HACCP-Risk Assessment), on several occasions as pioneers in the industry. Similarly, PharmaVision has been recognized with many awards such as the Responsible Care and Environmental Awards of the Istanbul Chamber of Industry as well as those by CEFIC, the latest being the European Environmental award. The company has demonstrated its social responsibility on several occasions, but most notably through the construction and maintenance of an elementary education school in Düzce, an earthquake damaged region of the country.

Consequently, several multinational companies have chosen PharmaVision as their manufacturing partner in Turkey for their local and export markets.

Pfizer Turkey

Integration to New Pfizer "Right First Time" Initiative

Pfizer Turkey was established in 1957 in Istanbul which is the industrial capital of Turkey. At the beginning, the plant was designed to manufacture only a few products. In parallel to the pharmaceutical market growth in Turkey, the Pfizer plant also has extended its manufacturing capacity to satisfy the increasing demands in years.

In 1993, penicillin and cephalosporin plants became operational; within a short period of time, these two facilities became the most important driving forces of Pfizer Turkey in its export business mainly to the Eastern European markets.

In 2005, the company exports 17 different pharmacy and animal

Case Studies

health products to 24 markets around the world. Ninety percent of export sales go to the Eastern European Region countries which are mostly EU members such as Poland, Czech Republic, Hungary, Slovakia, and Lithuania.

In 1995, the non-penicillin manufacturing facility also was renovated to ensure current GMP compliance requirements. The company continues to invest in maintenance and quality improvements to assure its constant compliance status.

In 2004, Pfizer Turkey made export sales of $19 million. This alone constituted 7% of Turkey's annual export sales in the sub-sector of pharmaceutical products, declared to be amounting to $272.5 million by the Exporters' Union, Istanbul. With this figure, Pfizer Turkey ranked the third biggest exporter of the sector overall in Turkey and received an award in February 2005.

The export sales have been showing upward trend over the last few years. In 2004, the figure grew by 60% compared to 2003 and exceeded last years' performance by export sales of $23 million in 2005. Regarding the manufacturing capacity for the local markets, 37 different products are locally manufactured with the 148 presentations.

Taking in account the imported and toll manufacturing products, Pfizer Turkey supplied 121 different products with 356 different presentations with the total supply volume of 44 million packs in year 2005.

As an extension of various quality improvement tools applied over the years, the Right First Time (RFT) Strategy is a Pfizer Global Manufacturing (PGM) driven strategic initiative that will enhance effectiveness of the Pfizer Manufacturing core processes by quality and performance improvement projects.

Being a data driven strategy, RFT utilizes some statistical models. One of the basic tools of this strategy is the Six-Sigma, which has been widely used by the manufacturing and non-manufacturing industries as a problem solving, business process development, and a decision making technique based on real data.

Pfizer's Right First Time Strategy is established around Five Strategic Mission Elements

Organizational Initiatives

RFT will concentrate attention on relations within the Pfizer Global Manufacturing (PGM) organization between Active Pharmaceutical Ingredient (API) and Drug Product (DP), or between PGM and another Pfizer Division - Pharmaceutical Global Research and Development (PGRD), or external as in the case between PGM and their suppliers.

Paradigm Shift

Fundamental to RFT is the recognition that there is a paradigm shift occurring in the pharmaceutical industry. This is a shift that will move organizations from an empirical to a science-basis for manufacturing operations.

Colleague/Culture

Basing all actions on good scientific and risk-management principles, Pfizer Turkey believes that product quality and performance is foremost achieved and assured by design of effective and efficient manufacturing processes. Therefore, product specifications are based on a mechanistic understanding of the relevant formulation and process factors.

The recognition of the need for the right persons in this project led to a major effort in Pfizer Turkey to select and develop suitable colleagues for this project. The result has been the achievement of the Right First Time culture on a broad basis.

Process Understanding

Process Analytical Technology (PAT) is the driving force for process understanding.

Because the process understanding was one of the most important key factors for the successful completion of the RFT projects, Pfizer Turkey has started to use several PAT applications in RFT projects. One major example is the use of NIR spectroscopy for better process understanding and more effective and efficient incoming material analysis for quality control purposes.

Performance

Pfizer's Right First Time initiative was started primarily to increase the quality of services and products. Within the past two years with the successful integration of new global initiative several Right First Time projects were successfully completed which contributed to increase the effectiveness and efficiency of Pfizer Turkey's manufacturing and supply operations.

With the help of global performance metrics and knowledge sharing activities, sites in different countries find a chance to compare and improve the capability of the processes.

Pharmaceutical Associations and Organizations in Turkey

ISPE Turkey Affiliate
Kusbakisi sok. No: 29 B Blok
Altunizade/Uskudar Istanbul,
Turkey
Tel: +90-212-482 0000 (2601)
Fax: +90-212-482 0086
E-mail: info@ispe.org.tr
www.ispe.org.tr

The Republic of Turkey, Ministry of Health
Mithatpasa Cad. No: 3
Sihhiye Ankara, Turkey
Tel: +90 (312) 435 6440
Fax: +90 (312) 4339885
E-mail: info@saglik.gov.tr
www.saglik.gov.tr

ISPE Turkey Inaugural Meeting
8 December 2005

Chemical, Petroleum, Rubber, and Plastic Industries Employers Association of Turkey
Kusbakisi sok. No: 29 B Blok
Altunizade/Uskudar Istanbul,
Turkey
Tel: +90-216-651 4900
Fax: +90-216-474 9192
E-mail: kiplas@kiplas.org
www.kiplas.org

Pharmaceutical Manufacturers' Association of Turkey
Talatpasa Cad. 98/B Gultepe
Istanbul, Turkey
Tel: +90-212-278 8540
Fax: +90-212-2787007
E-mail: info@ieis.org.tr
www.ieis.org

Turkish Pharmaceutical Industry Association (TISD)
Yildiz Posta Cad. İs Bankasi
Bloklari B Blok D: 1
34349 Esentepe Istanbul, Turkey
Tel: +90-212-275 9630
Fax: +90-212-274 5024
E-mail: info@tisd.org.tr
www.tisd.org.tr

AIFD (Research-Based Pharmaceutical Companies Association)
Barbaros Bulvari No: 121, TEV
Orhan Birman İs Merkezi
Balmumcu Istanbul, Turkey
Tel: +90-0212-267 1600
Fax: +90-212-273 1179
E-mail: aifd@aifd.org.tr
www.aifd.org.tr

YASED (Foreign Investors Association)
Barbaros Bulvar1 Mürbasan Sok.
Koza Is Merkezi
B Blok Kat.1 Balmumcu /
Beşiktaş Istanbul, Turkey
Tel: +90-212-272 5094
Fax: +90-212-2746664
E-mail: yased@yased.org.tr
www.yased.org.tr/