


AIFD 2016 ANNUAL REPORT

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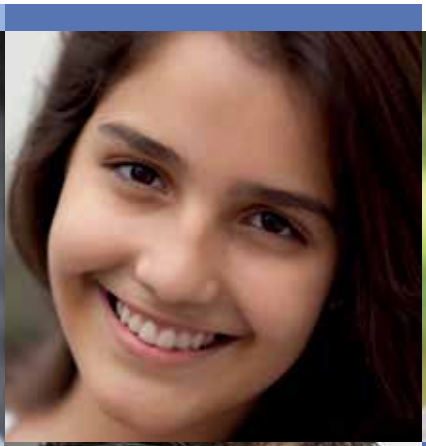
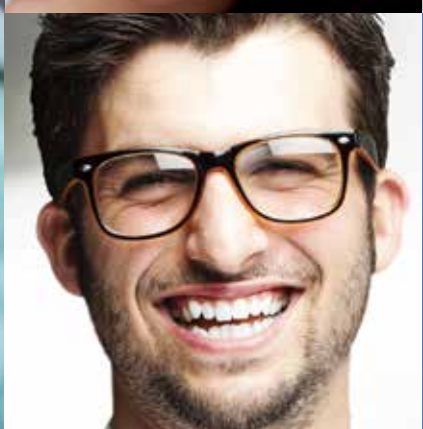
ARAŞTIRMACI İLAÇ FİRMALARI DERNEĞİ

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Members


abbvie

ACTELION

ALEXION

Allergan

AMGEN

astellas

AstraZeneca

B BRAUN
SHARING EXPEXPERTISE

BAUSCH+LOMB

BAYER

Boehringer
Ingelheim

Bristol-Myers Squibb

Celgene

Chiesi
Sağlık İçin Yenilikçi Fikirler

Daiichi-Sankyo

Eczacıbaşı

Shire

FERRING
PHARMACEUTICALS

FRESENIUS
KABI

Gen
İlaç ve Sağlık Ürünleri

GILEAD
Advancing Therapeutics.
Improving Lives.

gsk

İbrahim Etem
1903
MENARINI group

Johnson&Johnson

Lilly

Lundbeck

MERCK

MSD

NestléHealthScience

NOVARTIS

novo nordisk

NUTRICIA
Advanced Medical Nutrition

Pfizer

Roche

SANOFI

SERVIER

Takeda

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Message from the Chairman and the Secretary General

Dear Members,

As the Association of Research-Based Pharmaceutical Companies (AIFD), which continues to operate with the mission of improving the access of patients in Turkey to innovative medicines and treatments and ensuring an "ethical and transparent" business and working environment since our establishment in 2003, we have left behind another remarkably intensive year. As the Board of Directors elected in the 13th Ordinary General Assembly held on February 12, 2016, we would like to present the summary of the work we have carried out in 2016.

The AIFD stands out as a respectable and active civil society organization operating in the field of healthcare in Turkey over the last 15 years. Largest contribution enabling the AIFD to reach this position belongs to AIFD member companies that invested in Turkey by believing in the potential and future of this country, provided employment, offered their global knowledge and experiences at the disposal of the people in our country and generated value for the people, patients and economy of this country. We owe our esteemed members a sincere gratitude for all the support provided until today for enabling the AIFD to reach this point.

2016 has been a year in which we set our priorities as the AIFD through a holistic approach, shaped our organization and working principles in line with these set priorities, pursued our activities within the framework of a roadmap developed in this direction and put into practice relevant actions. As in previous years, we worked in close cooperation with all our stakeholders, being the first and foremost public authorities in 2016.

Prior to the 13th General Assembly held in February 2016, we held a two-day strategy workshop with the participation of the General Managers of all companies represented at the AIFD. The six key priorities on which we reached a consensus following this workshop were: pricing and financing of pharmaceuticals, market access and reimbursement, investment climate, building and governing AIFD perception, promoting the voice of patients and caregivers and protection of intellectual property rights. We defined actions and outputs addressing each key priority. Following the General Assembly, we redefined our working structure and system as the newly elected Board of Directors, in accordance with these six key priorities. We increased the number of Strategic Management Committees (SMCs) to five, which generate strategic content within the AIFD and put this content into action and communicate it, accordingly undertaking the following

Dr. Mete Hüsemoğlu
Chairman of the Board of Directors

roles: "Access SMC" responsible for the pricing and funding of medicines, "Investment SMC" responsible for investment policies, "Regulatory and Intellectual Property Rights SMC" responsible for regulatory framework and intellectual property rights, "Corporate Communication SMC" responsible for AIFD's corporate communication activities and "Ethics and Compliance SMC" responsible for ensuring and maintaining an ethical and transparent business and working environment. Consequently, each SMC was entrusted with the tasks assigned in line with the actions relating to these priorities. You may find in this annual report the details of what we have done as the AIFD vis-à-vis all these key priorities in this.

We believe that we have worked in a much more effective and productive manner through this focused approach in 2016. We also carried out a "Member Satisfaction Survey" for the first time to identify how our activities are regarded by our esteemed members. We believe that the outcomes of this survey will provide us very valuable clues on what can be done better from now on.

We would like to present a brief account of 2016 vis-à-vis our key priorities set for 2016 as well as the topics of major importance for our sector in our agendas in 2016.

We welcome the efforts put in parallel with global developments and trends, with the concern of the achieving sustainability of healthcare services, aiming to control healthcare expenditures. However, we have expressed in various occasions that the pharmaceutical market to remained stagnant or grew marginally, while continuing to grow in volume, results in a policy option that is far from being sustainable for the industry.

We continued to put an uninterrupted effort in 2016 for the establishment of a sound and sustainable system relating to the pricing of medicines the number one priority item in our key priorities. With this regard, we were actively involved place especially in the processes related with the drafting of the new pricing decree and notification, in cooperation with the other civil society organizations of our sector as per our deliverables set in our priorities. Although we are aware of the fact that we still have a long way to reach a fully sound and sustainable pricing structure, we acknowledge that at least a more predictable system is in place.

Looking back, 2016 will be remembered probably as one of the most challenging years all over the world. When we lay aside the economic and social problems experienced on a global scale, the atrocious coup attempt we experienced in Turkey, which was prevented by the Turkish Nation's taking ownership of democracy, was the most important event of the year for us. As the AIFD, we were active throughout this process particularly in terms of promoting the sustainability of the investment and business environment. We enabled the communication of positive messages on Turkey via all our international stakeholders and thus managed to preserve a

Dr. Ümit Dereli
Secretary General

positive perception regarding our country in the global public opinion, particularly in terms of the business and investment environment. One of the most important reflections was the Pharma-Vision 2016 meeting held in Ankara on September 27, 2016, with the participation of Deputy Prime Minister Mehmet Şimşek. Especially as the voice of the global pharmaceutical industry, the representatives of EFPIA and PhRMA confirmed once again very strongly the trust they have in Turkey and their commitments for this country in this meeting.

As the AIFD, we will continue, as we have done so until today, with our communication and efforts in all areas of pharmaceutical policies in line with the priorities and actions to be determined by our members and elected Board of Directors in order to fulfill our responsibilities. Our hope and goal is to achieve a climate where the patients in Turkey access the most developed treatments at the same time with the patients in the developed countries across the world and where the pharmaceutical industry realizes its investments in a predictable and sustainable business and working environment. To ensure the establishment of such climate, we will continue in the new term to pair up the technical know-how and expertise of the pharmaceutical industry with the active contribution and support of our members to generate value for each and every stakeholder.

Sincerely,

Dr. Mete Hüsemoğlu
Chairman of the Board
of Directors

Dr. Ümit Dereli
Secretary General

Board of Directors and Board of Auditors

The Board of Directors

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Chairman / AbbVie

Dr. Emin Fadıllıoğlu
Deputy Chairman / GSK

Şebnem Girgin
Vice Chairman
Gilead

Elif Aral
Vice Chairman
Pfizer

Dr.Peter Desmond Catalino
Vice Chairman
Novartis

Dr.Pelin Eriştiren Incesu
Controller / Astra Zeneca

Muhittin Bilgütay
Member
Baush & Lomb

Jose Daniel Lucas Guerrero
Member / Lilly

Adriano Antonio Treve
Member / Roche

Fabrizio Guidi
Member / Sanofi

Hatice Kurtar Demiray
Member / MSD

The Board of Auditors

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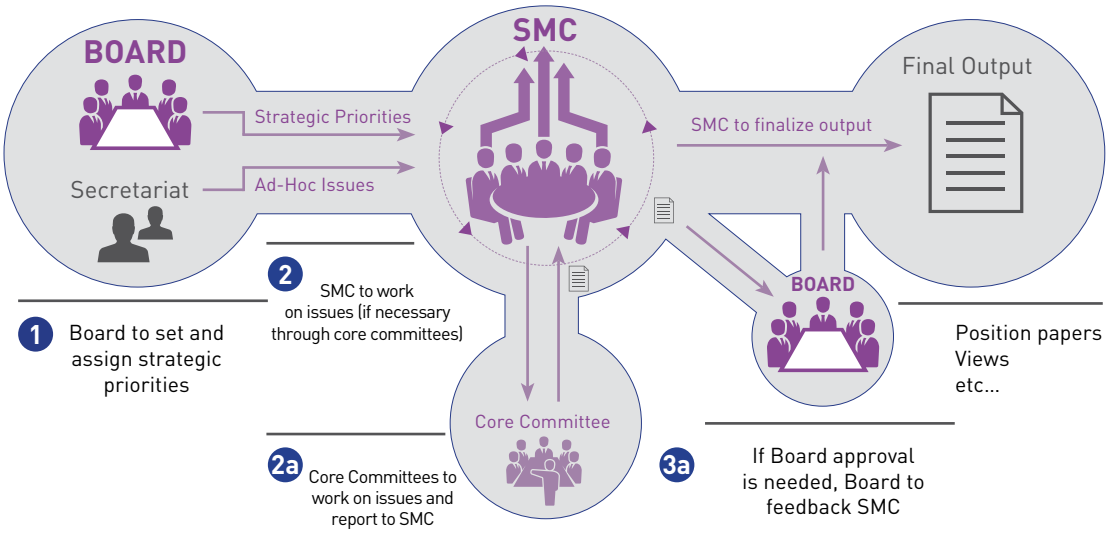
Member / UCB

Uğur Bingöl
Member / I.E. Ulagay

Dr. Oğuz Mülazımoğlu
Member / Bayer

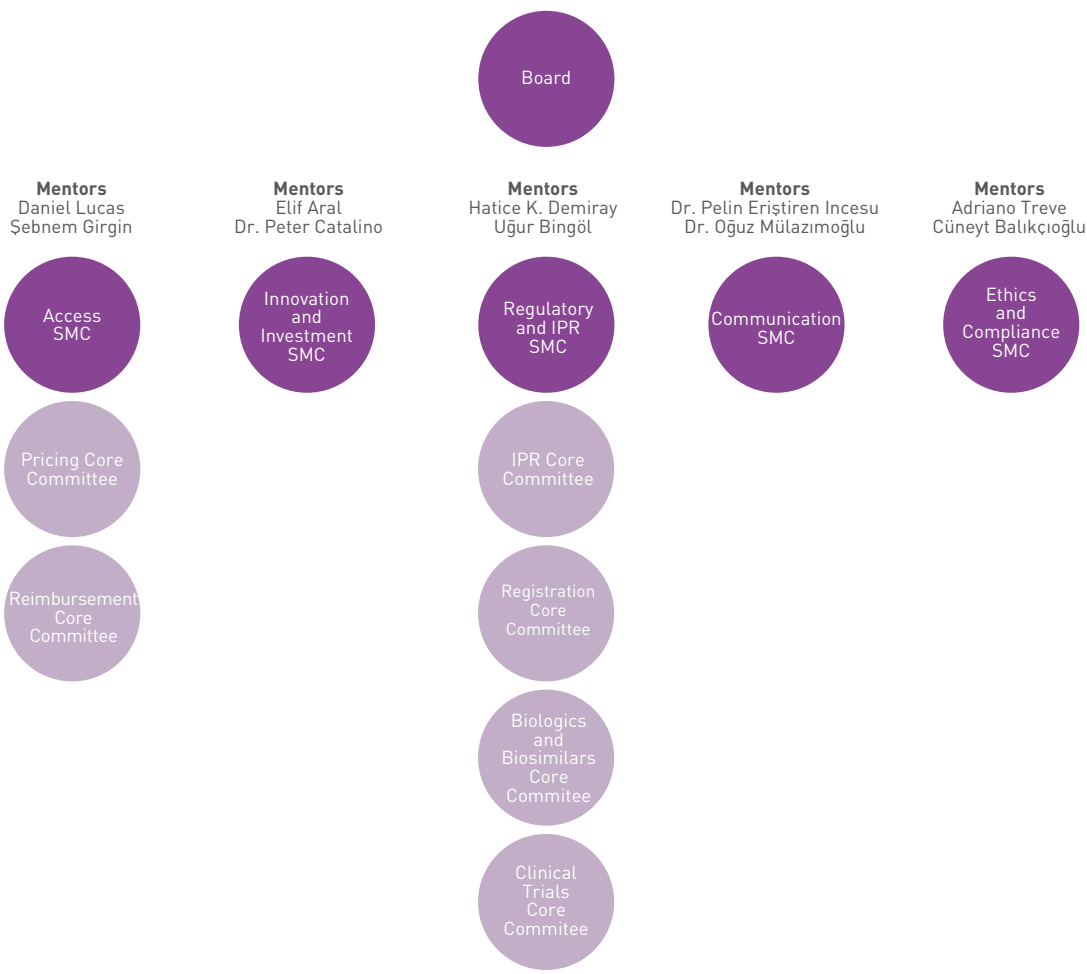
AIFD WORKING BODIES

AIFD Governance Model



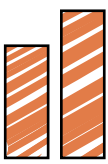
BOARD: Board of Directors
SMC: Strategic Management Committee

AIFD Working Bodies



FACTS AND FIGURES

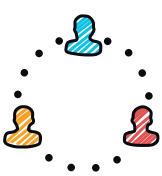
16
Turkey's position in the global pharmaceutical market ranking



1/50
Proportion of the Turkish pharmaceutical market compared to the pharmaceutical market in the US

%20
Share of original products with no generics in the reimbursed market

384 million Turkish liras
Amount of clinical trial investments made by AIFD members in 2016



476
Number of clinical trials conducted by AIFD members in 2016

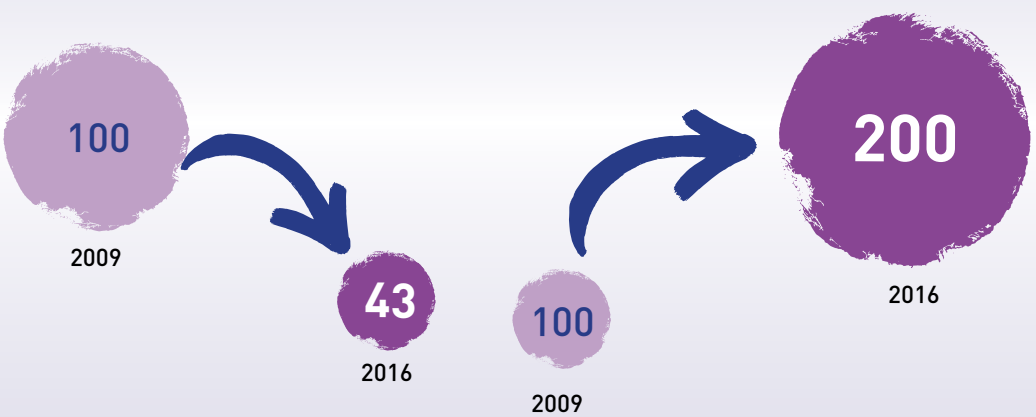
%15.5
Nominal growth of the pharmaceutical sector in 2016

While Turkey is placed in the 16th position in 2016,
it is expected to **climb up by 2 places in 2021 and become the 14th** largest market.
The ratio of the Turkish pharmaceutical market to that in the US is 1/50.

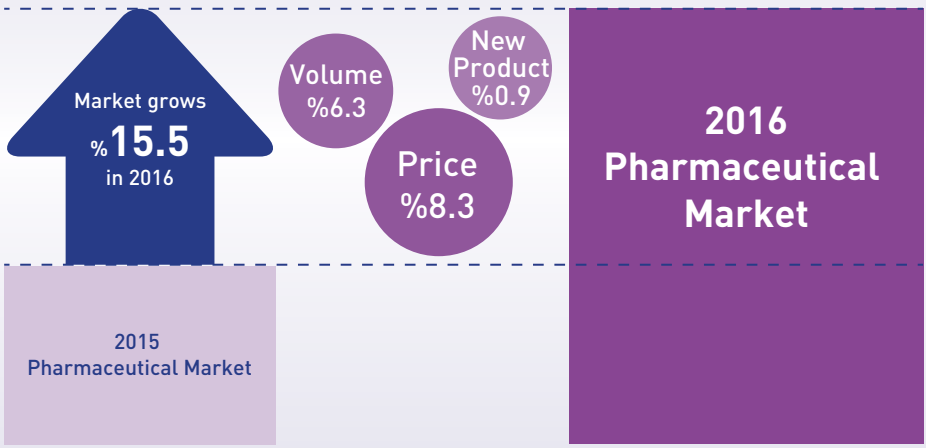
Exhibit	2016	Index
1	U.S.A	100
2 ▲1	China	26
3 ▼1	Japan	19
4	Germany	10
5	France	7
6	Italy	6
7	U.K	6
8 ▲2	Brazil	6
9 ▼1	Spain	5
10 ▼1	Canada	4
11 ▲2	India	4
12	Australia	3
13 ▼2	South Korea	3
14 ▲1	Russia	3
15 ▼1	Mexico	2
16 ▲5	**Turkey**	**2**
17 ▼1	Poland	1
18 ▲6	Suudi Arabia	1
19 ▲2	Argentina	1
20	Switzerland	1

Exhibit	2021	Index
1	U.S.A	100
2	China	25
3	Japan	14
4	Germany	8
5 ▲3	Brazil	6
6 ▲1	U.K	6
7 ▼1	Italy	5
8 ▼3	France	5
9 ▲2	India	5
10 ▼1	Spain	4
11 ▼1	Canada	4
12 ▲1	South Korea	2
13 ▲1	Russia	2
14 ▲2	**Turkey**	**2**
15 ▼3	Australia	2
16 ▼1	Mexico	2
17 ▲1	Suudi Arabia	1
18 ▼1	Poland	1
19	Argentina	1
20 ▲7	Egypt	1

While prices **dropped by 57%** in real terms since 2009, the **volume doubled**



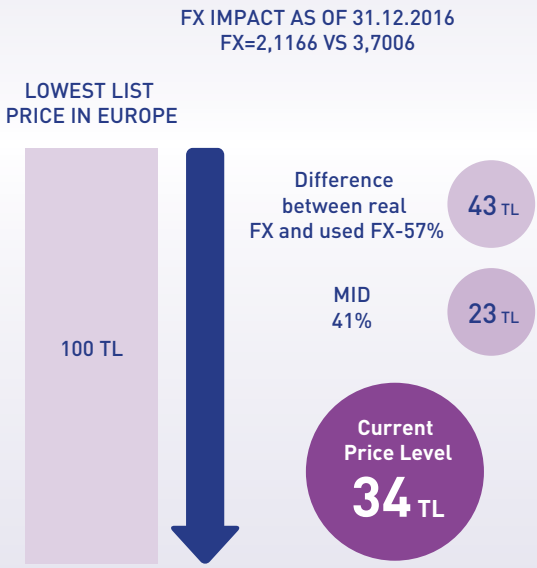
The pharmaceutical market grew nominally by 15.5% in 2016.
8% of the growth is price related and **6% was volume related.**
The impact of new product introduction was 1%.



The growth of innovative pharmaceutical companies: 11.2%

As of the end of 2016,
Euro exchange rate utilized in the pricing of medicines is **43%** below than real foreign exchange rate

Therefore, an innovative medicine in Turkey loses **2/3** of lowest Europe price due to difference in exchange rate and discounts.



Turkey Drug Distiribution Chain

Source: AIFD calculations based on the IMS database.

According to EU R&D Scoreboard, the global R&D investment of pharmaceutical companies amounts to 132.3 Billion Euros.

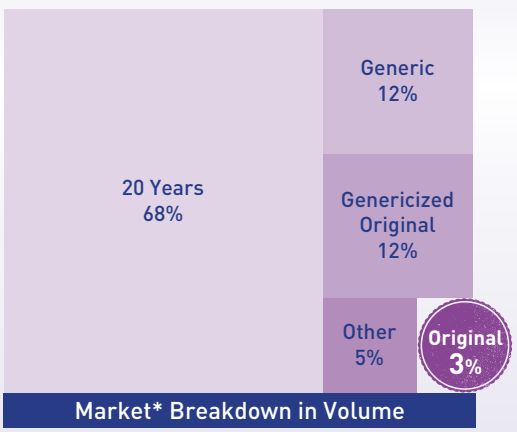
AIFD members represent 75% of this investment and allocate 17% of their turnover to R&D.

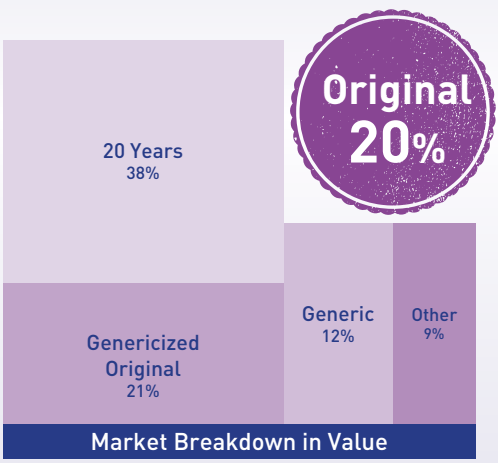
In 2016, AIFD members made an investment of 384 million Turkish Liras in total (115 million Euros) with 476 clinical trials conducted in Turkey.

12 of the trials conducted are at Phase I.

While original products constitute only 3% of the reimbursed market, two out of each three products are 20-year-old products.

In value terms, original products constitute 20% of the market.





*Reimbursed pharmacy market

INNOVATION, TURKEY AND THE AIFD IN 2016

Innovation	Turkey	AIFD
January		
University of Washington developed a pen-sized microscope which can distinguish between cancerous cells and normal cells. Scientists succeeded in achieving real-time and three-dimensional images of the growth and movement of a cancerous tumor for the first time. Italian Neurosurgeon Sergio Canavero successfully performed a head transplant on a monkey.	The Medium-Term Program (2016-2018) was published. The Ministry requested the capacity status of the companies manufacturing in Turkey. Meeting on the evaluation of manufactured equivalent medicine groups was held.	AIFD's Board of Directors convened with the Minister of Labor and Social Security, Süleyman Soylu. AIFD visits in Brussels. AIFD was represented at the Pharmaceutical Assembly of Turkish Union of Chambers and Commodity Exchanges (TOBB).
February		
Scientists reported an "unprecedented" success by using T cells for treating cancer. In one study, 94% of the symptoms of acute lymphoblastic leukemia patients disappeared completely. It was discovered that pancreatic cancer has four subtypes each based on a different reason and requiring a different treatment.	The regulations comprising the working procedures and principles of the "Pharmaceutical Reimbursement Commission", "Alternative Reimbursement Commission" and "Medical and Economic Evaluation Commission" were published on the Official Gazette. The Euro exchange rate, taken as basis in pricing, was increased from 2.0767 TL to 2.1166 TL.	Başak Yılmaz joined the AIFD. The Pricing Notification Meeting between TITCK and the Sector was held. AIFD's Strategy Meeting with General Managers was conducted. AIFD's General Assembly was held.
March		
German researchers identified a specific gene which may reduce the risk of heart attack by 50 percent in humans. Researchers at the University of Toronto announced that they used stem cell treatment for reversing age-related osteoporosis in mice.	The announcement on the "Localization Process" was published and the commission on imported to manufactured products was established. The presentations particularly on the "prioritization of registration" and "localization" were shared with the representatives of the sector in the consultation meeting held between TITCK and the Sector.	A consultation meeting was held between TITCK and the Sector. AIFD was represented at the 7th Rheumatology Congress. Luncheon was conducted with Prof. Dr. Recep Akdağ within the scope of the Meetings with the Sector at Acıbadem University.

April

Scientists shared an updated "biological tree of life", summarizing the evolution of all known living things until today.

The Clinical Trials Symposium of the Turkish Public Hospitals Institution was conducted.

Visits were carried out by EFPIA Director General within the scope of his contacts in Ankara.

May

Researchers discovered new findings indicating that the amyloid-beta protein acts as a natural antibiotic in the brain. They reported that Alzheimer's associated amyloid plaques could constitute a normal part of the immune system and that removal of amyloids could actually be harmful.

The "Registration Prioritization" guidelines were published.

The Extraordinary Convention of the Justice and Development Party was held and the 65th Government was established with Binali Yıldırım as Prime Minister.

The Meeting Between TITCK and the Sector and the Pharmaceutical Convention was held in Istanbul.

The Workshop on Alternative Reimbursement SEPD and SGU was carried out.

June

A new combination of chemotherapy medicines for pancreatic cancer, presented at the largest cancer conference worldwide, demonstrated that long-term survival could be extended from 16% to 29%.

The meeting on "Biosimilar Products" was held at TITCK with broad participation.

TITCK requested a GMP inspection application dossier is submitted to the Agency for the imported products registered prior to March 2010.

Dr. Çetin Değer joined the AIFD.

AIFD established contacts in the US within the framework of the BIO Convention.

AIFD's Board of Directors met with Minister of Finance, Naci Ağbal.

July

NASA astronaut Kate Rubins sequenced DNA for the first time in space in the International Space Station by using the MinION sequencer.

A coup attempt took place on July 15.

S&P cut Turkey's credit rating to below the investment level.

Cengiz Aydın joined the AIFD

August

It was demonstrated that Aducanumab, a new antibody, significantly reduced harmful beta-amyloid plaques in patients with early stage Alzheimer's disease.

Meeting was held between TITCK and the Pharmaceutical Sector on the Evaluation of Pricing Applications for Medicinal Products for Human Use

AIFD Head Office was renovated.

September

The result of the DNA testing performed on a selection of skeletons in London confirmed that Yersinia pestis was the bacteria responsible for the plague of 1665.

The Carbon Dioxide (CO2) level increased consistently since the Industrial Revolution, breaking records over and over in recent years. However, the CO2 level of 400 ppm was passed worldwide.

The announcement on "Combination Products in Which the Identical Mono Forms Contained in Each Active Substance Are Included into the Reimbursement List" was published by SGK (80% decision).

Law No. 6745 on Supporting Investments on a Project Basis and Amending Certain Laws and Decree Laws.

IPTS Congress was held.

AIFD's Board of Directors met with the Minister of Health, Prof. Dr. Recep Akdağ.

The report entitled "Pharmaceutical Products and Export in Turkey", prepared in cooperation by the AIFD and Economic Policy Research Foundation of Turkey (TEPAV), was launched.

The Pharmaceutical Vision 2016 meeting, graced by Deputy Prime Minister Mehmet Şimşek and attended by many representatives from the pharmaceutical sector in Europe and the US, was held.

October

2016 Nobel Prize for physiology and medicine was presented to the Japanese Yoshinori Ohsumi for his discoveries related with autophagy.

It was demonstrated that one-year survival rate with Nivolumab was more than twice higher in head and neck cancer compared to current therapies. Furthermore, it also reduces tumors in patients with advanced stage kidney cancer.

The reimbursement list of Terms 2nd and 3rd terms in 2015 were published.

The Symposium on Rational Drug Use was held.

The Medicines and Medical Devices Agency of Turkey signed a cooperation protocol with Ankara University on biotechnology training.

A "Data Sharing Protocol" was signed between SGK and MoH.

AIFD representatives and the representatives of other associations in the sector visited the Minister of Labor and Social Security, Dr. Mehmet Müezzinoğlu.

AIFD's Board of Directors visited the Minister of Labor and Social Security, Dr. Mehmet Müezzinoğlu.

November

The mini lungs grown in a laboratory setting from stem cells were successfully transplanted into mice by researchers at the University of Michigan.

Large-scale testing of a potential HIV vaccine began in South Africa.

Inspection was introduced for non-prescription medicines following the amnesty for stocks.

A new reform process was initiated in the field of healthcare.

AIFD established contacts with ISPOR

IMS Client Day was conducted.

Joint meeting of the American Chamber of Commerce and AIFD's General Managers was held.

December

A study revealed that a vaccine 70-100% effective against the Ebola virus was discovered. Thus, it was reported that this was the first proven vaccine against this disease.

The National Health Service (NHS) of the United Kingdom reported that 10 blind patients will receive 'bionic eyes'.

The application fees, annual fees, transaction fees and contract fees to be paid to the Social Security Institution were updated.

A cooperation protocol was signed between SGK and the National Post and Telegraph Directorate of Turkey.

Meeting between the AIFD and the Health Media was held.

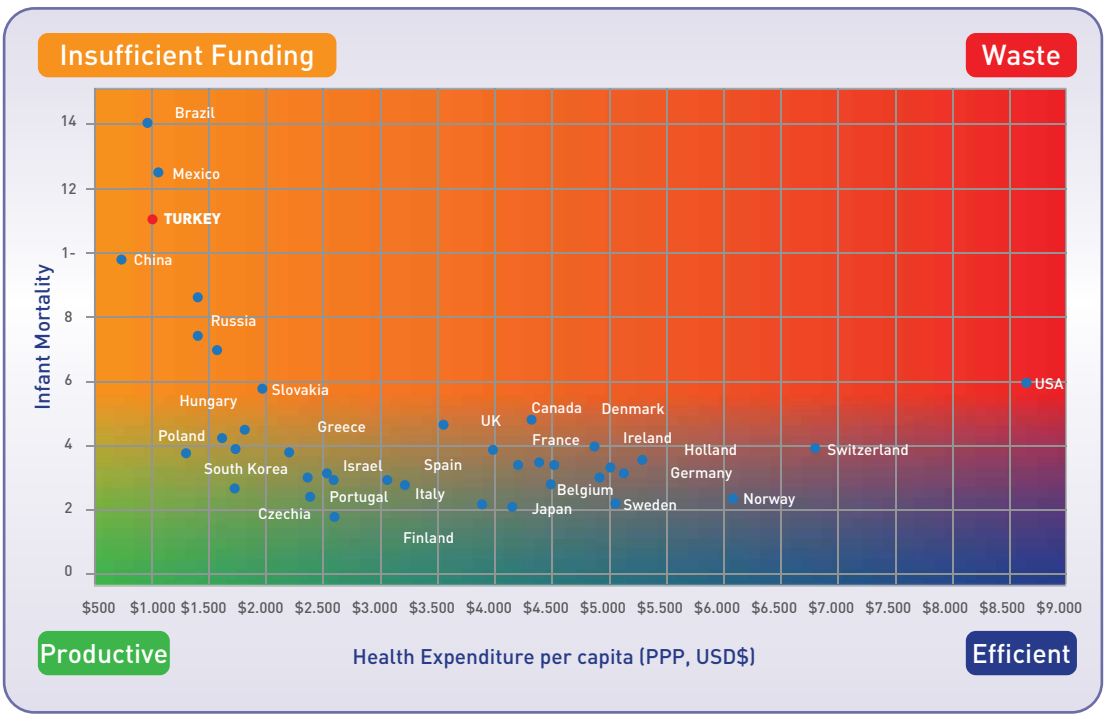
Joint meeting between the AIFD and Vice Presidency of the Inspection Services Department of TITCK was held.

Meeting between the AIFD and Patient Associations was held.

HEALTHCARE AND DEVELOPMENT

Healthcare constitutes the core of economic and social development in Turkey. With the first programs for transformation in healthcare, Turkey achieved in 8 years the progress made by OECD countries in 30 years. However, aging population, increasing antibiotic resistance and rising burden of non-contagious and chronic diseases still continue to be among the priorities of decision-makers.

While the progress achieved in the first phase of transformation in healthcare enabled catching up of the health indicators of developed countries in many fields, there is need to increase also the resources allocated for healthcare in order to write a new success story.



While seeking for ways to increase its health outputs, Turkey also strives to achieve sustainability of its financing. Rational drug use stands out as a key instrument from this respect. The public pharmaceutical budget was designated as 21 billion Turkish Liras in 2016 and the year-end realization is estimated to reach nearly 22 billion TL according to the calculations of the AIFD.

It is necessary to accelerate the provision of innovative therapeutic options to patients in Turkey and avail of more predictable processes in the access to healthcare financing. It takes approximately 30 weeks on average for innovative medicines to be accepted to the reimbursement system. 2016 has been a year of major developments from many aspects.

Alternative Reimbursement Models

Right at the beginning of 2016, the regulations comprising the working procedures and principles of the "Pharmaceutical Reimbursement Commission of SGK", "Alternative Reimbursement Commission of Universal Health Insurances of SGK" and the "Medical and Economic Evaluation Commission" were published on the Official Gazette within the framework of the national pharmaceutical policy.

According to the new regulation, it was planned for the commissions to work on the production of export-oriented medicines, the inclusion into the reimbursement list of strategic products such as products of vital importance, to be procured from abroad due to not being registered in Turkey and which are used in rare diseases, the encouragement of the production of high-technology products not manufactured or not available in Turkey and of the transition of imported products to local products, the adoption of relevant decisions for supporting local medicines and putting the decisions into practice. The number of reimbursement periods was lowered from three to two with the new regulation.

Particularly in relation with the working principles and procedures of the Alternative Reimbursement Commission, it is noted that the implementation scope and terms as well as the foreseen procedure are vague and, thus, it is necessary to clarify the implementation.

In 2016, 494 products were included into the positive list, 6 of them through alternative reimbursement models.

The medicine groups on which Alternative Reimbursement models may be applied need to be clearly identified. Considering the definition of the alternative reimbursement model in the regulation, it is concluded that alternative reimbursement models will be implemented according to the financial or medical benefit to be provided and in terms of the product and service groups procured from abroad which cannot be manufactured or are not available in our country.

The general principles regarding applicable Alternative Reimbursement Model(s) have not been designated. Within the scope of the Regulation, no specification was made regarding the general principles on which companies could have a preliminary idea and which they need to observe. Although the terms relating to the alternative reimbursement model will actually be designated by the contracts to be signed between relevant companies and SGK, it will be beneficial to make the Regulation put forth the general principles of alternative reimbursement models and indicate by name some alternative reimbursement models in order to provide guidance. Besides the inclusion into the scope of reimbursement upon providing purchasing guarantee, it is not possible to foresee what other alternative reimbursement models may be.

AIFD's visit to the Minister of Labor and Social Security, Dr. Mehmet Müezzinoğlu, October 2016

There is no certainty on the timing and details of the process. One of the most fundamental components of the alternative reimbursement system is the need for the process to operate rapidly. However, the provisions of the Regulation do not include any arrangement regarding the timing of applications and evaluation of alternative reimbursement process.

The implementation needs to be clarified regarding which documents and materials are required at the application phase. The participation of the relevant company into the process is left to the discretion of the Commission. In case service is requested from universities/training and research hospitals and their employees, placed as third parties in the designation of the reimbursement model, also companies should be included into the evaluation processes of the results of the service provided.

Yet, it is stipulated in the regulation that it is the duty of the Commission to "designate and adopt decisions on the draft contracts to be signed with companies for the reimbursement model" and that the representatives/authorities of companies will participate in the meetings of the Commission "where deemed necessary". However, it should be obligatory for company representatives to participate at each meeting where a decision will be adopted regarding the contract to be signed.

There is no certainty regarding how the relationship between the alternative reimbursement system and the current reimbursement system will be. It is specified in the regulation that in case a healthcare product or service is included into the alternative reimbursement list, it will be considered whether the other therapeutic options included into the scope of reimbursement will continue to be reimbursed. The other therapeutic options included into the "current" reimbursement list may be removed from the reimbursement list.

SGK 2017-2019 Strategic Plan, February 2017

2.4-Generation of policies directed at the development of healthcare insurance	**2.4.1** Development of supportive models in healthcare insurance	**2.4.1** Number of alternative contracts signed in line with the alternative reimbursement regulation with providers of medical supplies used for in-patient treatment
	2.4.2 Development of rational reimbursement models	**2.4.2** Number of alternative reimbursement models for the medicine
	2.4.3 Development of effective pricing policies	**2.4.3** Number of activities (seminars, conferences, projects, etc.) carried out in relation for the effective use of the lines of healthcare providers
	2.4.4 Realization of work related with the effective utilization of the lines of healthcare service providers	**2.4.4** Number of activities directed at the development of the production of healthcare technologies in Turkey and the use of domestic products
	2.4.5 Realization of work directed at the development of the production of healthcare technologies in Turkey and the utilization of domestic products	

Performance Indicators

	Performance Indicators	2017	2018	2019
P.G.2.4.1	Number of alternative contracts signed in accordance with the Alternative Reimbursement Regulation with the providers of medical supplies used for in-patient treatment	5	10	20
P.G.2.4.2	Number of alternative reimbursement models for the medicine	1	1	1

In case it is not possible to sign an alternative reimbursement agreement or termination of the agreement, the fate of the healthcare service constituting the subject matter of the agreement is not clear either. Under normal circumstances, it is expected and even necessary that the "current" reimbursement system is implemented.

In conclusion, the referred provisions need to be clear so that they are not used as compulsory tools by the Agency against companies.

Rational Drug Use

2016 was a year in which the awareness towards rational drug use displayed growth. Due to its responsibility as a stakeholder, AIFD also carried out activities and developed solution proposals on "rational drug use" which holds an important place also for the Ministry of Health.

In line with its mission, AIFD aims to ensure that medicines are used in the most efficient and effective way by patients and thus conducted work directed at unveiling areas of potential financial efficiency. Antibiotic resistance is a globally accepted health condition: it is estimated that 10 million people will lose their lives annually by the year 2050. The causes of antibiotic resistance are listed as follows:(i) presence of a positive correlation between the use of antibiotics and the prevalence of resistance development, (ii) non-rational and uncontrolled use of antibiotics, (iii) the fact that antibiotics are not used at the adequate dose and period by patients, disruption of the treatment regimen, (iv) commercial concerns of pharmacy establishments...

Antibiotic resistance is growing in Turkey and Turkey is ranked 2nd after Greece among countries where antibiotic resistance develops most. Meanwhile, Turkey is placed in the first position among OECD countries in terms of antibiotic use. In light of these facts, Turkey took up an adequate problem within the framework of rational antibiotic use.

Despite the bans on direct sales in 2015, the sales of antibiotics without prescription continued at a notably high level. The oral antibiotic market grew, while the number of prescriptions remained the same. However, the annual unit sales of antibiotics surpassed the annual prescription projection by 35%. Thus, we welcome the amnesty introduced in stocks and consider it as a milestone. All of the medicines in the stocks of pharmacies will be tracked by the Drug Tracking System (ITS) records, simultaneously with TITCK. It is important to use the right arising from the relevant legislation when we detect that they are sold without prescription, starting with these product groups.

Activities directed at generating awareness on antimicrobial resistance via effective communication and trainings should continue. In the reported published by the World Health Organization, it was identified that "the commercial concerns of pharmacies nurtured excessive and erroneous use of antibiotics". Within this framework, we propose that the implementation of "free goods" is banned in this area.

Considering current treatments on the basis of a multinational surveillance study, it is possible to save 155 million TL annually in total by writing prescriptions line with guidelines and taking into account also growing development of antibiotic resistance. Therefore, in addition to the trainings directed at rational antibiotic use provided by the Ministry of Health in our country, country-specific guidelines and treatment protocols should also be designated.

WHO proposes that the infection prevalence directed at the prevention of antibiotic resistance is reduced via access to healthcare, hygiene and preventive healthcare services. The vaccination level in children reached a high rate as 95% in Turkey; however, considering the needs of Turkey, investments intended for vaccines, novel medicines, diagnostic tools and other interventions should continue to be supported and adult vaccination programs should be developed considering the risk groups.

Antimicrobial management programs should be applied also in hospitals. Hospital based antibiotic resistance surveillance data and antibiotic treatment protocols should be established and all clinics should initiate treatment in light of this protocol.

Moreover, infection control committee should operate more effectively, sub-committees should be established, where necessary, for hospital based antibiotic management and regular surveillance based trainings should be provided by hospital acquired infectious diseases specialist to other clinics (surgery, etc.).

Transparency practices regarding promotional activities should be rolled out in the sector. The sector should undergo self-inspection (as in the AIFD's Code of Practice Panel); inspection and sanction mechanisms (e-prescription, disclosures of transfers of value, congress participation notifications, etc.) should be established and implemented in light of the information available at the Ministry. Furthermore, the certification of promotional representatives should be widespread and followed up by the Ministry and the private sector. Particularly the procedures and principles of the relations with HCPs and Healthcare Organizations should be very well defined.

Nowadays, there are diagnostic and treatment protocols prepared in many countries and on many topics in relation with Treatment Guidelines. The enforcement of the principles regarding the preparation and use of diagnostic and treatment protocols will increase rational drug use. These principles (i) should be prepared on the basis of being evidence-based, as stipulated by guidelines and protocols and the document should be drafted by a relevant Specialized Association or Professional Society, (ii) the protocols should be providing guidance and not be compulsory, (iii) indication restrictions violating generally accepted treatment guidelines worldwide should not be implemented.

Support should be provided to Rational Drug Use policies with pharmaceutical industry support programs. One of the most frequently observed issues in chronic diseases is treatment non-compliance and, according to the World Health Organization, only 50% of the patients receiving treatment take their medicines as they should. Severe symptoms occur as a potential consequence of treatment non-compliance and patients require a more aggressive treatment, while their quality of life is reduced. This results in an increase in work load and stress for physicians and to an escalation of difficulties in their communication with patients. Disease progression, increase in hospital admissions also means an increase in treatment costs due to the increase in the work load of physicians. Finally, it leads to a misperception in patients and physicians regarding the efficacy of medicines for pharmaceutical manufacturers.

The number of patients with a chronic condition will increase due to aging population and this will generate a larger burden over the system. It is believed that patient support programs will reduce the burden over the system due to the increase in treatment compliance in this area. Furthermore, the adverse events reported via patient support programs will provide a major contribution in ensuring the utilization of medicines in a safe manner. Our proposal regarding this topic is that a working group is established to analyze the factors impacting the compliance of patients to the treatment in chronic diseases in Turkey, designate the impacts of the current situation on Rational Drug Use and formulate the action plans directed at the enhancement of treatment compliance. It is important that pharmaceutical manufacturers, healthcare organizations conducting patient support programs, physicians and patients are represented in this study group.

Combination Products

Work directed at the pricing of combination products in particular was frequently brought up in the second half of 2016. In the formal talks held in June, it was shared that it was planned to reduce the multiplier constituting the basis of reimbursement price application of fixed dose combination products, corresponding to 95%, to 80%. With the amendment in multiplier declared via the announcement of SGK in September, it was disclosed to the sector that the

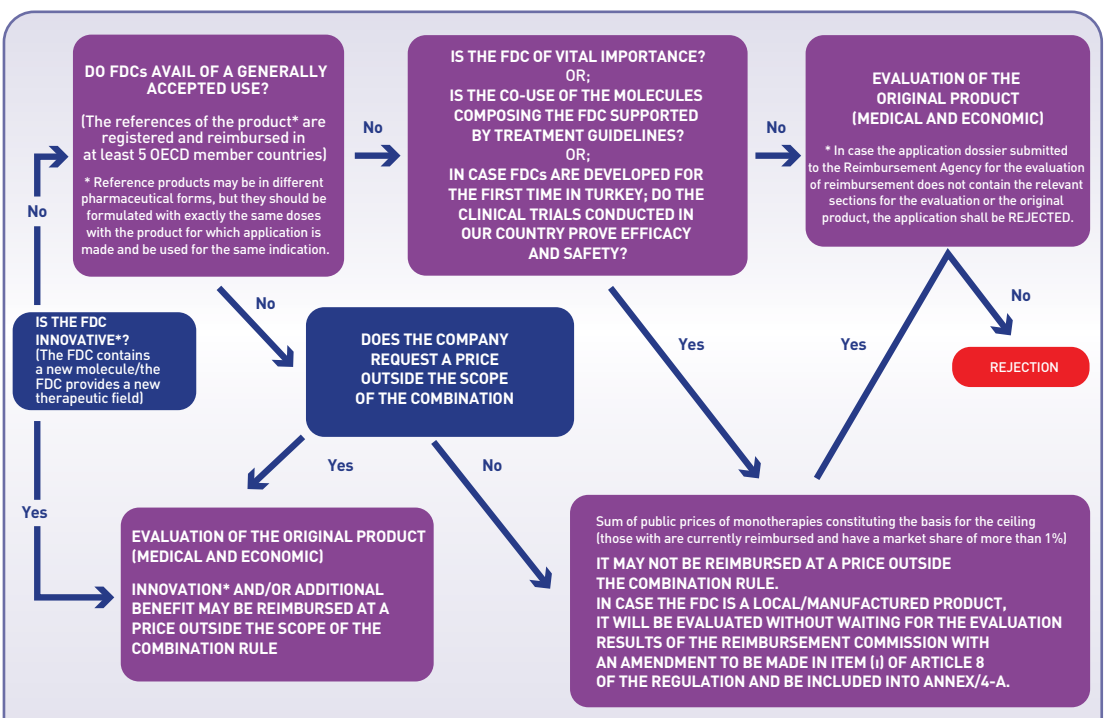
declared unit price would be sought also in this group of combination medicines currently included into the reimbursement list of the Agency (List of Medicines to be reimbursed).

The main objective in the fixed dose combination treatment is to reduce the number of medicines taken by patients, facilitate their treatment and thus increase patient compliance and reduce the costs related with low treatment compliance. It was confirmed also by the HTA report published by the Turkish Ministry of Health that particularly in cases where there is no budgetary impact, fixed dose combination use will enhance patient compliance, lead to a positive impact on disease control and thus contribute positively to the reduction of morbidity and mortality in chronic diseases. The point to be underlined here is that in case of non-availability of fixed dose combinations in the market, it is estimated that the expenditures to be made for the medicine groups into which they are included may be realized at a higher rate ranging between 2 to 15%.

Therefore, the imposition of additional arrangements to result in price reductions in order to achieve budgetary savings on these medicines the prices of which are arranged with the reference pricing system and the implementation of standard Public Institution discounts, as with all medicines, will jeopardize market availability of these products.

Hence, according to the announcement shared in December as a result of the meetings held between the Agency and the representatives of the Agency, the enforcement date of the implementation regarding combination products, announced to begin as of 01.01.2017, was postponed until further notice and the enforcement date, timeline and process relating to the implementation will be indicated in this announcement.

Although it is shared with the sector that savings amounting to 170 million TL will be obtained from combination products in 2017, the burden that may rise as a result of the removal of combination products should be calculated. We request that this topic is assessed again with the participation of all stakeholders.



Reimbursement Evaluation Process Algorithm of Fixed Dose Combinations, AIFD, 2016

PATIENT AND HEALTH

The priority of the pharmaceutical sector has always been placed on humans. Many people live a healthier life as a result of the years-long research of scientists, studies of clinical teams and the risk undertaken by entrepreneurs. The need for healthcare services increases by changing shape with aging population and the pharmaceutical industry continues to invest in research and innovation despite market access restrictions and price controls in order to enable future generations live even a healthier life.

Pricing

2016 was a year when the changes made in the previous year were implemented for the first time and the work directed at the need for simplification in the pricing legislation were initiated. The Q&A meeting regarding the implementation of the pricing notification, which became effective towards the end of 2015, was held in Ankara in February where the need for amendments (simplification) in the notification was mutually expressed for the first time.

In the visits realized in July, it was reported that the work related with the notification would be initiated soon and that the first informative meeting would be held in August. Particularly the non-notification of price changes of up to 3% created additional work load for TITCK from an operational perspective and the fact that it would not be included into the updated legislation was shared with the sector already in July. The authorities of TITCK convened with the representatives of the sector in Istanbul on August 24 and provided information on their work. AIFD mostly continued with the work conducted in 2015 and shared them again with the Agency.

The need for a new approach towards pricing was expressed also by the Minister of Health in the meeting held in September.

Towards the end of 2016, the pricing notification and decree were shared with the sector to receive their views. The drafts which introduced new price controls, reductions, additional operational burdens and amendments in definitions, along with many major changes, were regarded as unacceptable from many angles for all representatives of the sector.

The amendments proposed included the topics of having a reference pricing system expanded in a manner so as to comprise all PIC/S member countries, introducing a 20% price reduction for biological products, pulling down the ceiling price of non-reimbursed medicines to the level of reference countries with a low reference and changing the definition of 20Years products and thus restricting their price protection. AIFD decided to act in tandem with IEIS and TISD throughout the whole process and objection was made categorically against these changes so as to ensure the sustainability of the system.

AIFD Board of Directors' visit to the Minister of Health, Prof. Dr. Recep Akdağ, September 2016

A consensus was approached as a result of the meetings held in December with the Minister of Health and consequently again with the Agency representatives of TITCK

As the AIFD, we request, first of all, for the correction of the 70% multiplier within years in order to achieve a sustainable pricing system. The difference between the real foreign exchange rate and the exchange rate taken as basis in pricing is currently close to 60%.

Furthermore, we also believe that some arrangements, which may relieve the system and not impose an additional budgetary burden, may be performed. In order to further strengthen the impact of the foreign exchange rate which is significantly different as indicated above, not reflecting the decreases in reference price until the difference in foreign exchange rate is offset will provide a major improvement.

Morever, if decreases arising from reference price do not surpass 20% within a year, this will enhance predictability for companies and reduce at least at a certain degree the risks arising from low prices. Dependency on the prices of reference countries, which is another vulnerability brought by the international reference pricing system may impact also Turkey due to special circumstances experienced in those countries. In previous years, the condition of countries such Greece, which went bankrupt, poses a risk also for the Turkish pharmaceutical market. Therefore, we believe that it will be an appropriate step to add the article for freezing the reference country position on a temporary basis for countries under special circumstances.

Many micro-challenges were faced in pricing in 2016. The signature process of the Decision Amending the Pricing of Medicinal Products for Human Use was completed just one day before the expiry date (February 22) of the new Euro value (2.1166 TL) and the price brackets were increased in proportion with the increase in foreign exchange rate, thus eliminating the question marks on the last day.

AIFD Board of Directors' visit to the Minister of Health, Prof. Dr. Recep Akdağ, September 2016

Again, the price increases granted by the Price Evaluation Commission on the price list were annulled in April. The cross exchange rate price increases granted to products regarded as critical according to articles 3-4 and 5-1-a of the notification dated 2012 and which received product specific price increases and the products whose country of import was not a Euro country were revoked.

It was recorded by TITCK on April 18 that another country with a price lower than the price of the reference country was identified for two products and that thus amendment would be made in the notification. It was shared with the authorities of the Agency that, in relation with the search for the cheapest medicine price on a global scale, the medicine prices in Turkey were currently too low and that no margin was left for further decrease in this system which already operated with difficulty.

Sector's view was requested in June regarding the amendment the definition of 20Years products. According to the referred amendment, if the Agency had previously considered that it would be suitable for only one active substance to be introduced into the market before 1987 for instance in combination products with two active substances and a 20Years status was granted to that product, this will no longer be possible with the proposed amendment.

According to the decision of the Price Evaluation Commission (FDK) of January 3rd, 2017, the Euro value used in the designation of medicine prices was amended as 1 ₤ =2.3421 TL. However, Turkey is one of the countries with the lowest medicine prices worldwide. Today, the value of 1 Euro corresponds to approximately 4 TL. The Euro exchange rate used in the pricing of medicines was increased to 2.3421 with the arrangement made on January 6. As per the referred decision, price changes will become effective 45 days following the date of arrangement; that is, on February 20.

Registration and Inspection

The pharmaceutical industry in Turkey experienced major legislative amendments and decisions in 2016. One of the major amendments was the publication of the "Guidelines on the Working Procedures and Principles of the Commission for the Priority Evaluation Commission of Medicinal Products for Human Use" (Prioritization Guidelines)" in May.

These guidelines define the evaluation and process to be carried out by the Priority Evaluation Commission on the products included into the list of Applications to be Prioritized in Registration Process.

Also the prioritization of the applications for Good Manufacturing Practice (GMP) inspections is defined in these guidelines.

As a result of the evaluations conducted by the Commission, applications are designated as "highly prioritized", "prioritized" and "with normal priority".

It is aimed to complete the registration procedures in 150 days in "highly prioritized" products and in 180 days in "prioritized products". But, no timeframe was indicated for the registration procedures of product "with normal priority". Yet, according to the Registration Regulation of Medicinal Products for Human Use, the registration period of medicinal products for human is designated as 210 days.

According to a survey carried out among AIFD members: The median registration period for the applications finalized as of the end of July 2016 is 469 days.

The average registration period of actively tracked applications (according to survival analysis projection) is 659 days, while the median period is 604 days.

The median period elapsed at the Medicines and Medical Devices Agency (TITCK) is 259 days in completed applications, this period reaches 448 days in the survival analysis projection.

Within the scope of the Registration Regulation of Medicinal Products for Human Use, taken as basis in the registration of products in our country, there is an arrangement enabling products which are "the first in treatment or diagnosis and introduce an innovation" to be evaluated within the scope of prioritized/accelerated registration procedure, solely on the basis of these characteristics.

However, considering the Prioritization Guidelines, the Retail Sales Price (TL) and Public Sales Price (TL) declarations requested for innovative medicines and the demand for commitment for these prices should be evaluated together with the criteria of "being the first in treatment or diagnosis and introducing an innovation" with the objective of "reducing public health expenditures".

Meeting between the AIFD and TITCK's Inspection Department, December 2016

It is noted that there is a representative also from the Social Security Institution in the Priority Evaluation Commission.

The prioritization process envisaged with the Guidelines comprises the pricing and reimbursement processes and this arrangement covers not only registration, but also the areas of pricing and reimbursement due to the Retail Sales Price and Public Price commitment required to be completed especially for the applications of innovative medicines and the applications for medicines included into the list ıf medicines procured from abroad. The fact that the product is evaluated based on the impact on public finance during the registration process excludes this process from the scope of being medical/scientific evaluation process.

AIFD organized regular meetings throughout the year to achieve mutual sharing of knowledge and experience within the scope of Turkey-EFPIA Regulatory Network and benefitted from this "know-how" in these activities.

Comparing with other health authorities;

Out of 157 registered products, 83% of products were registered by Europe, 68% of products were registered in the US.

It takes 2 years for the application to be completed.

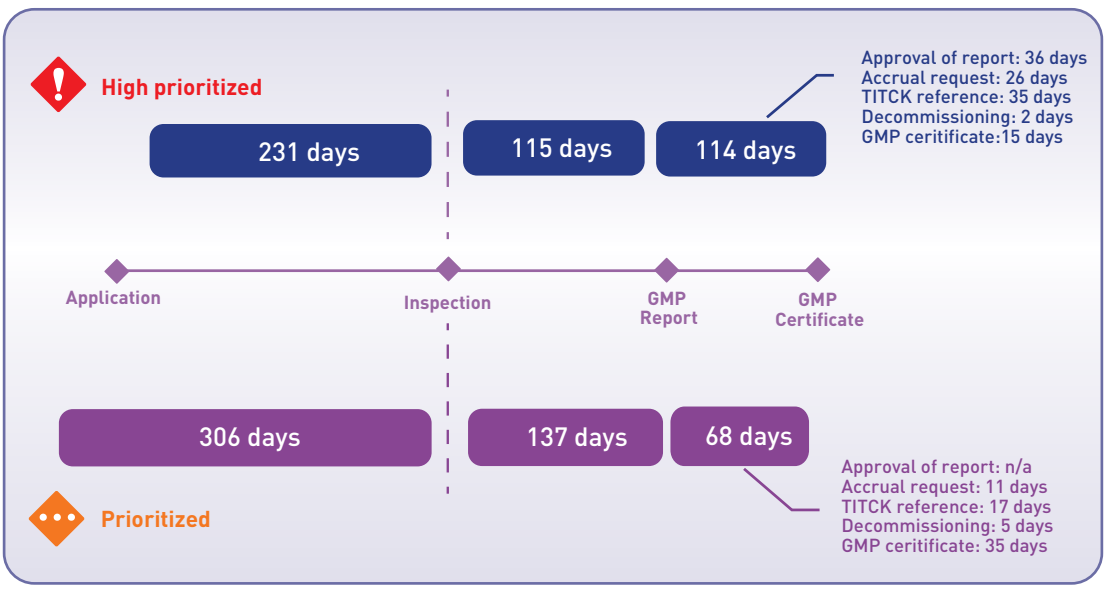
Good Manufacturing Practice (GMP) Inspections

This year, GMP inspections constituted another important agenda item for the AIFD. AIFD positions were brought up by the AIFD in the sectorial meeting held with TITCK's Inspection Department, held most recently in December 2016.

AIFD & TITCK Meeting, December 21, 2016

Due to the increase in the number of GMP application dossiers and re-certification applications throughout the years, the request also for GMP inspection applications in the products registered prior to 2010, the registration of highly prioritized and prioritized products within targeted periods (150 and 180 days) and, finally, the increasing number of facilities undergoing multiple inspections, it is necessary to make a transition from line-based inspections to site-based inspections.

The scope of parallel applications should be expanded so as to comprise also prioritized products together with highly prioritized products.

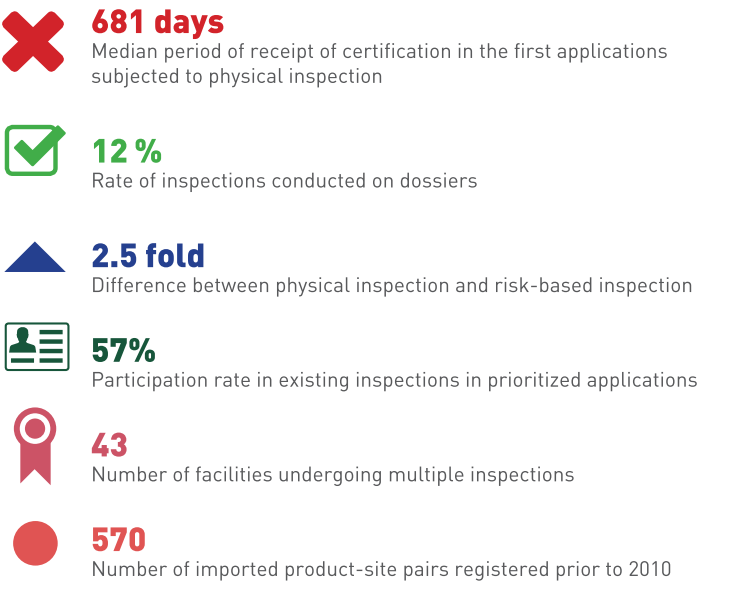


Physical GMP inspections last 97 weeks on average and this period in 2.5 times longer than risk-based inspection. Meanwhile, the rate of inspections carried out based on the dossier remains only at 12%. On the other hand, considering physical inspections, it was identified that 43 facilities underwent multiple inspections.

With the announcement made by TITCK in June 2016, request was made for the submission of application to the Presidency of the Pharmaceutical Inspection Department until 30.12.2016 for the conduct of the inspections of all manufacturing phases of all imported medicines products for human use registered prior to 01.03.2010.

The most important development regarding mutual recognition of GMP certificates is that thanks to the progress achieved in 2016 in TITCK's PIC/S membership process, membership is expected to be granted to TITCK in 2017. AIFD follows with great appreciation the steps taken by TITCK in this direction and offers any kind of support.

Another agenda item of the meeting held between TITCK and the AIFD in December was Pharmacovigilance Inspections. Active participation was achieved in this meeting and actions were taken for the improvement of processes. Our feedback relating to signal management and safety variations were submitted to TITCK and it was observed that the relevant guidelines published at the end of 2016 included these improvements. The Pharmacovigilance video prepared by a member company was communicated to the whole sector by TITCK and its utilization in congresses and similar meetings was ensured. In line with such type of projects providing a major contribution to our awareness activities, the first item in the goals and priorities of 2017 will be our other activities aimed at enhancing awareness.



AIFD Survey on GMP Inspections, December 2016

Biological Products

The weight of biological products rises in Turkey as in the rest of the world. According to a study by IMS, 10 out of 20 most valuable medicines in development phase are biosimilar medicines. In light of these developments, TITCK initiated efforts directed at the fulfillment of legislative requirements this year.

A biosimilar working group was established within the framework of TITCK. Fourteen members of this working group began to attend the post-graduate program in biotechnology at Ankara University, while five people were included into the staff from abroad for education purposes.

A meeting on "Biosimilar Products" was held in June in TITCK. The meeting was attended on behalf of the AIFD by the Chairman of the Board, Dr. Mete Hüsemoğlu, Board Members

Daniel Lucas and representatives from our member companies Pfizer, Amgen, Abbvie, Merck, Baxalta-Shire, Bayer, Sanofi, Roche, Lilly, Gen Ilaç, as well other representatives of the sector.

The views of the sector regarding the topics of "interchangeability" and "substitution" in biosimilar products were listened to in the meeting.

As indicated in AIFD's view regarding the Approval and Utilization of Biological Medicinal products, it is aimed to highlight the importance of understanding the value of all biological medicines, including biosimilars, in order to help develop the treatment and outcomes of patients. Biosimilars offer additional therapeutic options for physicians and patients and are currently available also in our country. As biosimilars are not the same with their reference products and cannot be considered as generic medicines, a separate and defined registration process is required for them.

All clinical data of biosimilar products should be evaluated upon taking into account the legislations and approaches of EMA, FDA and WHO and whether the biosimilar product is introduced into the market after being approved by these authorities. As evaluation is made on a product basis, molecule-specific guidelines should also be published.

The Summary of Product Characteristics of a biosimilar product should clearly indicate that the product is a biosimilar, explain or present the comparative studies carried out for proving its biosimilarity (e.g.; its indication) and, show, where available, the indications from which extrapolation was made.

Interchangeability should be granted only in line with clinical trial data designed only to prove interchangeability. The final decision regarding that treatment will be used by a patient should be adopted by the physician. The individual needs of patients can best be evaluated by their physicians. Patients should be adequately informed during this process and be aware they are receive a biological product prescribed by their physician upon evaluating the following aspects: all current therapeutic options; potential risks and benefits of different treatments; differences between products - for instance, different administration devices and the need to monitor adequately the safety and efficacy of the new treatment – for instance, the patient's antibody count, preparation of clinical records and measurement of clinical outcomes via patient surveys...

Biosimilars and reference biological medicinal products should not be subjected to substitution. The policies to be pursued in this area should observe and ensure freedom of clinical option and the physician's right for freedom of treatment; thus, the continuation of the treatment should be allowed and physicians and/or patients should be offered the flexibility of requesting the biological product they have chosen based on medical reasons. The topic of pricing of biotechnological and biosimilar products was brought up within the scope of the work on TITCK's decision and notification regarding the Pricing of Medicinal Products for Human Use in 2016 and AIFD's view on the need for not making any amendments in the relevant article and position was communicated to decision-makers.

According to draft report of IVEK BIO, held on January

2. PRICING AND REIMBURSEMENT

2.1. The prices of biotechnological products and biosimilars should not be decreased. The pricing rules stipulated in the current notification should apply.

2.2. Medicine prices in Turkey are irrationally low. Further reduction of prices will lead to non-availability of these medicines in the country.

IVEK BIO, January 2017

2.3. Biotechnological and biosimilar medicines should be promoted as this is a newly developing sector. Positive discrimination should be made.

2.4. Prices are expected to decrease by competition following the new introduction.

2.5. The government should guarantee that pricing and reimbursement policies will not change in the mid term upon taking into account the size of the investments in this field.

2.6. Incentives may be provided upon granting a purchasing guarantee in local products.

2.7. The budget of non-registered medicines should be reduced. (Registration should be granted and price regulation should be performed.)

2.8. A rational drug study should be carried out on self-care products.

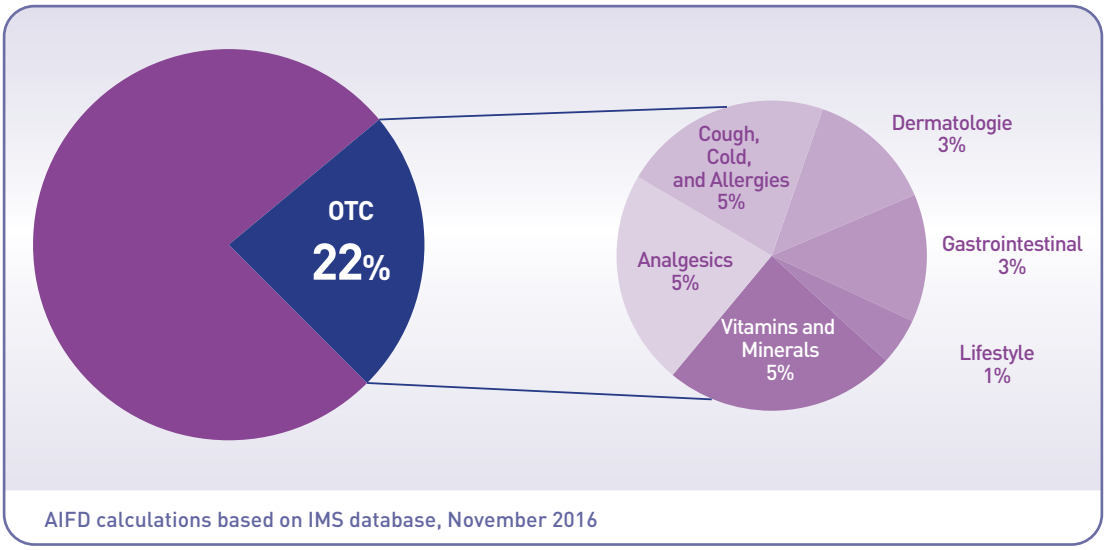
TITCK is expected to continue to work on the guidelines in 2017 as well. As the AIFD, we will continue to contribute to the work conducted. We continue to work in close cooperation with EFPIA and IFPMA for sharing international know-how with the Agency. Biological and biosimilar products became one of the permanent working units of the AIFD as of 2016 and the referred group continues to hold meeting periodically under the mentorship of the Board of Directors.

AIFD also participated in the second "Biologics Survey", organized by the European Biopharmaceutical Enterprises (EBE) and comprising 32 countries among which Turkey was included this year.

Nonprescription Medicines

2016 was a year in which various meetings and activities were conducted in the field of non-prescription medicines and importance of the regulation of this field was frequently highlighted by the Agency. Non-prescription medicines are regarded among the institutional priorities of TITCK and it is indicated that the legislation may be put into effect within 2017. This topic was frequently discussed in the meetings and congresses held in 2016 and will continue to be discussed also in the upcoming events.

AIFD believes that if conscious patients undertake responsibility regarding their own health and consult pharmacies for simple issues, this may enhance the efficiency of the healthcare system and make it possible for medical means to be utilized for chronic and more serious diseases. AIFD supports the guidance of the society and healthcare professionals in this field in order to achieve this as well as the revision of the current regulations within the framework of relevant guidelines and the enforcement of the arrangements.



AIFD calculations based on IMS database, November 2016

The classification of non-prescription medicines should be based on a consensus reached between the industry and healthcare authorities in accordance with the European and global classification criteria. The registration process of non-prescription medicines should be simplified and the GMP conformity of the products in this group should certainly be managed separately. The GMP inspection process for non-prescription imported medicines should be pursued in a manner so as to not constitute an obstacle for the registration and marketing of the product.

It is proposed that the provisions of the effective notification in the pricing of manufactured and imported non-prescription medicines are preserved and that a special implementation is put into effect for our country based on the examples from the European Union and the rest of the world, upon the enforcement of the legislation of non-prescription medicines.

It will be suitable to arrange and make free promotion to the public under certain conditions and regulate promotional and communication materials under the supervision of self-regulation or preliminary assessment channels. We support the arrangement of distribution channels in a manner so as to make pharmacies as the only distribution channel.

Upon the entry into effect of the legislation on non-prescription medicines, the relevant law will lead to the achievement of a major efficacy for the healthcare system in Turkey in terms of savings in pharmaceutical costs and the reduction of clinical burden, considering the limited financial resources and the status of human capital resources encountered following the initiation of the program for transformation in healthcare.

In addition to the recommendations provided by pharmacists to consumers regarding appropriate utilization methods upon controlling the consumption of non-prescription medicines, this will enhance the role of pharmacists as healthcare specialty in the society.

The arrangements made for non-prescription medicines will enable the achievement of an increase in the awareness of individuals to protect and manage their own health in our country as in the rest of the world, development of the healthcare literacy of the public and thus the information and promotion to be made towards the public will provide a major benefit for the facilitation of access to non-prescription products within this framework.

The legislative arrangement was brought up by Self-Care Products Association (SURDER) in the consultation meetings held between TITCK and the sector on March 7 and May 13. Important workshops were organized in this direction, together with public representatives, representatives of the sector and other stakeholders. Under the leadership of SURDER, the Workshop on the Draft Regulation on OTC-Healthcare Products was held first on May 31 and consequently on December 1 in Istanbul and another workshop entitled "Non-Prescription Medicines: Strategic Management Workshop" was organized by Turkish Pharmacists' Association (TEB) on November 3 in Ankara. All participants of the workshop agreed on the fact that the sole sales channel of non-prescription medicines should be pharmacies.

Ongoing work and plans were reflected also in TITCK's meeting with the sector in November and the news appearing on the press. According to the information shared, it was recorded that nearly 1,000 medicines would make transition to the status of non-prescription medicine. The categories indicated within this scope are cough, cold, allergy medicines, analgesics and antipyretics, gastrointestinal medicines, dermatological medicines, vitamins and minerals.

Another topic of importance for non-prescription medicines is the pricing of non-prescription medicines. Amendments were to be made in the pricing and price increases of non-prescription medicines in the draft pricing notification shared in November. The drawbacks of indicating the minimum reference price especially in the calculation of the real price and the implementation of the real reference price instead of the maximum reference price for non-prescription imported products/non-prescription products was shared with the authorities.

It will be possible to sell 15 percent of 13,000 medicines without prescription

Work has been initiated by the Ministry of Health for expanding the list of non-prescription medicines. It was reported that it will be possible to sell without prescription 15 percent of 13,000 re-classified medicines

Friday, November 25, 2016, Lütfi Erdoğan / DAILY HABERTURK

Rare Diseases and Orphan Drugs

In the consultation meeting held on March 7 between TITCK and the sector, AIFD was requested to work on a legislation for Orphan Drugs. The legislative work on rare diseases, included into the scope of the Turkish Pharmaceutical Sector Strategy Paper and Action Plan (2015-2018), aiming to enable patients access the medicines used in their treatment is a very valuable step. Thus, EMA and FDA legislations were harmonized and the AIFD's views, localized in line with relevant regulations in our country, were submitted to the Agency in May.

Consequently, some revisions were identified by TITCK and AIFD on the draft guidelines shared and the referred revisions were submitted to the Agency in July. One of the major topics on which we submitted our views was the need to grant the right to apply also the products registered on the enforcement date of the guidelines or for which registration application was made in order to be defined as orphan drugs. Also registered products, which could not be classified due to the absence of an orphan drug definition until today, should be granted the right to receive an orphan drug status with this regulation/these guidelines.

Furthermore, in order to ensure early access of patients to innovative medicines in Turkey, it is crucial to have an incentive policy (Market Exclusivity) for orphan drugs. In order to enable rapid access of orphan drugs to patients suffering from rare diseases in Turkey, a market exclusivity period should be defined for ensuring that patients suffering from rare diseases have continuous access to orphan drugs so that the sustainability of the companies operating in the field of rare diseases is ensured in Turkey and that investments intended for rare diseases endemic to Turkey are encouraged, in addition to the definition of orphan drugs.

AIFD's social media banner for Rare Diseases Day, February 2017

Market Access is one the most important incentive tools for orphan drugs in all developed countries such as the US, EU, Japan and Australia. Thus, in line with the EU "Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on Orphan Medicinal Products", we would like to request that; "In case registration is granted to a medicinal product for human use defined as orphan drug; no registration application shall be accepted for another product which is essentially similar for a period of 10 years as of the registration issuance date; in case of expiry of the first 5 years in the inability to grant registration and if there are concrete data indicating that the product does not fulfill defined conditions and that the product is commercially profitable, this period may be reduced to 6 years".

However, in addition to the submission of the registration applications for orphan drugs in parallel with the Good Manufacturing Practice (GMP) inspection applications for registration applications of orphan drugs, they should be evaluated as "highly prioritized products" for GMP inspection applications.

Regarding the pricing of orphan drugs, the definition of orphan drug should first be harmonized with the pricing legislation in line with the guidelines: "Medicinal products for human use developed in Turkey, or, where not available, in another country and/or region of the Caucasian race with maximum 5 patients per 10,000 people, against life-threatening, severely disabling or serious and chronic rare diseases or the research and development cost of which cannot be covered with sales figures even though they are intended for the treatment of maximum 5 individuals in 10,000."

Yet, in case orphan products are able to obtain a price of up to 100% of the reference price and where requested by the applicants, the possibility to grant a price of up to 10% more of the reference price in addition will contribute significantly to the availability of these medicines.

AIFD's social media banner for Rare Diseases Day, February 2017

INNOVATION

Innovation constitutes the core of the pharmaceutical sector. The treatment options offered by innovative companies enable people to live a longer and healthier life.

Intellectual Property Rights

Certainly, the greatest gain of 2016 in terms of Turkey's bringing the investment environment to a competitive position was the enactment of the law on Industrial Property Rights.

Patent protection in Turkey is provided in accordance with the Decree Law on the Protection of Patent Rights (Patent Decree Law), entered into effect in 1995. Turkey also became party to the Patent Cooperation Treaty in 1997 and the European Patent Convention in 2000. In line with clause 5, Article 90 of the Turkish Constitution, the referred international treaties are statutory in Turkey and are implemented directly. The obligation to review the National Patent Law increased due to inadequacy and conflicting nature of the provisions in the current Patent Decree Law, in the presence of the international treaties to which Turkey became a party in 1997 and 2000 and the rules put forth by the European Union Directives relating to Intellectual Property and especially Patent Protection – in line with the EU membership goal.

Finally, a Draft Intellectual Property Law, arranging all intellectual property rights under a single law, including also patent rights, was shared by the Ministry of Science, Industry and Technology in February. Close cooperation was achieved with all stakeholders of the public sector in this work initiated by our Government for the enactment of the "Intellectual Property Rights", which is one of the six strategic priorities of the AIFD in 2016.

An intense work was carried out in our Parliament for the draft law brought to the Turkish Grand National Assembly (TGNA) in June and the AIFD was represented in these meetings with our legal consultants. Also the know-how provided by EFPIA and PhRMA was reflected in our views conveyed in various platforms for ensuring compliance of the draft law with international standards.

As a result of all this work, the Industrial Property Law No. 6769 entered into force on January 10, 2017. Provisions on trademarks, geographical indications, industrial designs and finally patent rights are arranged by chapters one, two, three and four, respectively, of the law.

It should be underlined that in terms the provisions on patents, the new law introduces many provisions for ensuring that the national law is compliant with the European Patent Convention. The provisions on the rights of previous right holders, the utilization obligation of the patent and services inventions, stipulated in the Decree Law, are explained in a more explicit and comprehensible manner. Although the law introduced many positive arrangements in many areas, the arrangements introduced in relation with the "Obligatory licensing in case of non-utilization" carry a risk which may give rise to outcomes in conflict of the fundamental principles of legal certainty and protection of the rights of patent holders.

Data Exclusivity

Data exclusivity is arranged in accordance with the Regulation on the Registration of Medicinal Products for Human use in Turkey and the data exclusivity period is envisaged as six years starting from the first registration date in the Customs Union area. However, the fact that this period is initiated on the first registration date in the Customs Union area does not provide sufficient protection and, considering also the long ongoing registration processes in our country, it is observed that the 6-year protection granted in the regulation is not provided in practice.

Our proposal within this scope is that the data exclusivity period is revised in a manner so as to begin as of the first registration date in Turkey. Furthermore, we believe that the period granted in terms of data exclusivity should be arranged as 8 (eight) years in line with Article 10/1 of the EU acquis (2001/83/EC). Within the same scope, it is proposed that a market exclusivity of 2 (two) years is granted for products benefitting from data exclusivity.

Moreover, it is stipulated in the referred article that the data exclusivity period granted for products benefitting from patent protection in Turkey is restricted with the patent period. However, this is not a legally adequate arrangement. Because, the rights over the data subjected to data exclusivity and the rights over the patent(s) relating to the product are to separate rights. While the patent protects the invention as an intellectual property right, data exclusivity protects the data relating to clinical trials and test outcomes. In other words, as the rights relating to data are not protected with the patent right, the association of clinical trial and test data with the patent right does not comply with intellectual property law. Therefore, patent rights and data exclusivity rights should be preserved independently is separate periods and the protection period of one should not be restricted with the period granted for the other.

Within this scope, we propose for the correction of the relevant provisions in line with the EU Directive 2001/83/EC and the addition of the corrected version to the newly drafted regulation.

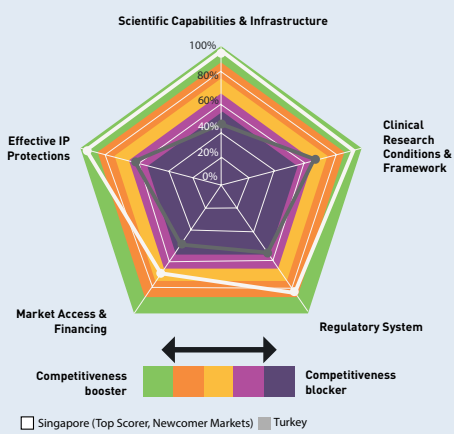
Clinical Trials

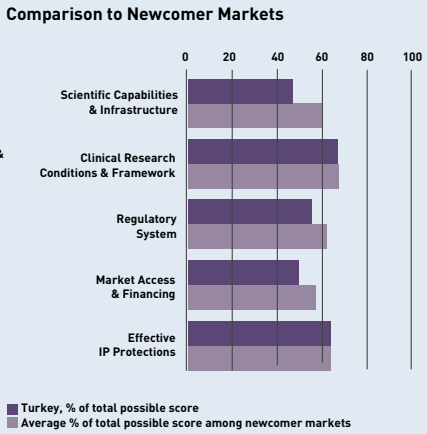
The main players of the innovation ecosystem are universities, research centers, public institutions, companies and entrepreneurs. Innovation emerges as a result of the interaction of these players with each other under suitable environment conditions. The conditions nurturing this ecosystem are composed of financial resources and incentive mechanisms, legal arrangements, education and human rights and the factors within the investment environment. Turkey avails of all the players composing the innovation ecosystem.

Considering the R&D value chain in Turkey, it may be seen that relevant players are present roughly for all stages and that the ecosystem are improving. The Structural Transformation Program declared within the scope of the latest 10th Development Plan, support different components of the relevant ecosystem intended for the development of R&D in Turkey.

Many research projects that may nurture pharmaceutical R&D are conducted in life sciences and health sciences at universities for discovery, basic research and preclinical studies which constitute the first phase of pharmaceutical R&D value chain. The amount of support provided to these projects increases, while new support programs are opened at the same time. In addition to the project supports provided for researches, an increasing number of relevant research centers were also included into the ecosystem. Financing sources were achieved in order to establish research infrastructures in a similar way to project supports. It is observed that these research infrastructures and projects are shaped in a manner so as

BCI Survey 2016 - Category Scores





Pugatch Consilium BCI, 2016

BCI Results In Depth: What helps and what hinders Turkey's biopharmaceutical competitiveness?

Scientifc Capabilities & Infrastructure

- ✗ R&D capabilities continue to be viewed as limited and collaborative R&D as remaining small in scale.
- ✓ New spending and incentive under the pharmaceutical strategy and recent bioclusters/ research centers are largely seen as positive developments.

Clinical Research Conditions & Framework

- ✗ Clinical trial apporoval deleays hold back inverstment in RYD. Hospitals and
- ✓ local CROs are viewed as having adequate capacity for cliniacal research.

The Regulatory System

- ✗ Regulatory delays (including due to difficult GMP rules) are still viewed as a asignificant challenge, with knock-on effeckts in other areas (such as market Access and IP).
- ✗ Executives report remaining gaps in regulators' capacity for drug review (thougt the qulaity control framework specifically as seen as satisfactory.)

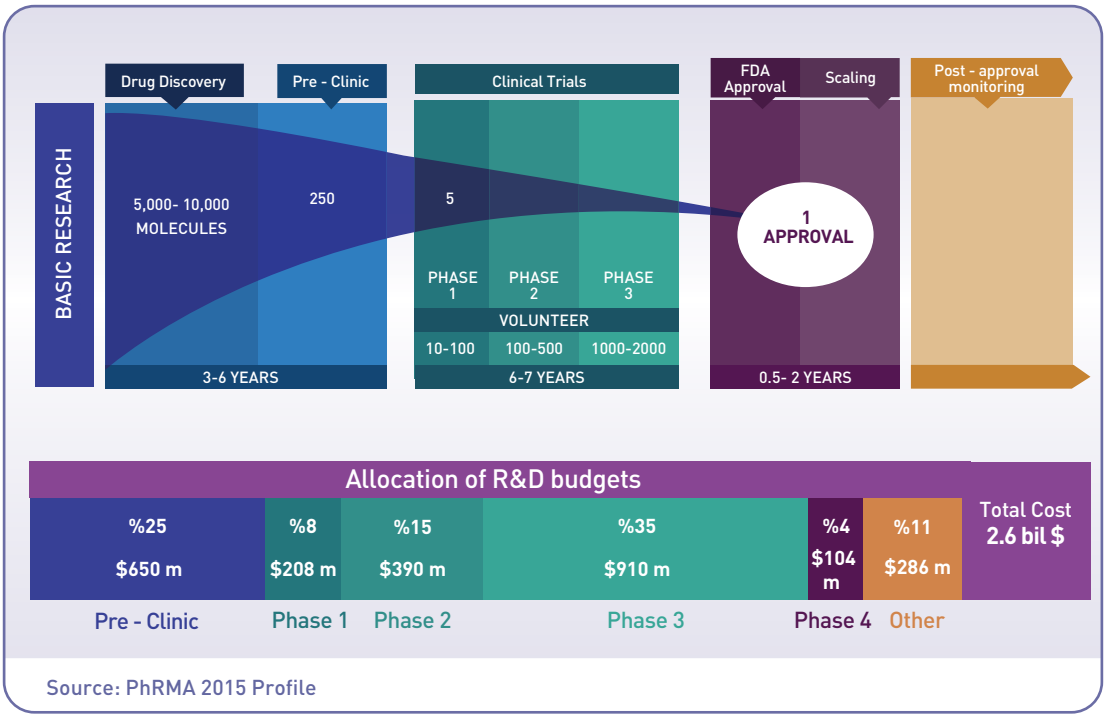
Market Access & Financing

- ✗ Concerns over localization and potential delisting of foreign products is present under a new government actian plan.
- ✓ Special Access programs are welcome but are currently very limited (and are seen as prioritizing local products.)

Effective Intellectual Property Protections

- ✗ Draft IP amendments are perceived as mixed, with potential for further deteriorstion.
- ✗ The RDP framwork and erosion of that framework due to registration delays still represents a barrier.

The current data exclusivity implementation constitutes a barrier in making Turkey competitive, Biocompetitiveness Index Pugatch Consilium 2016



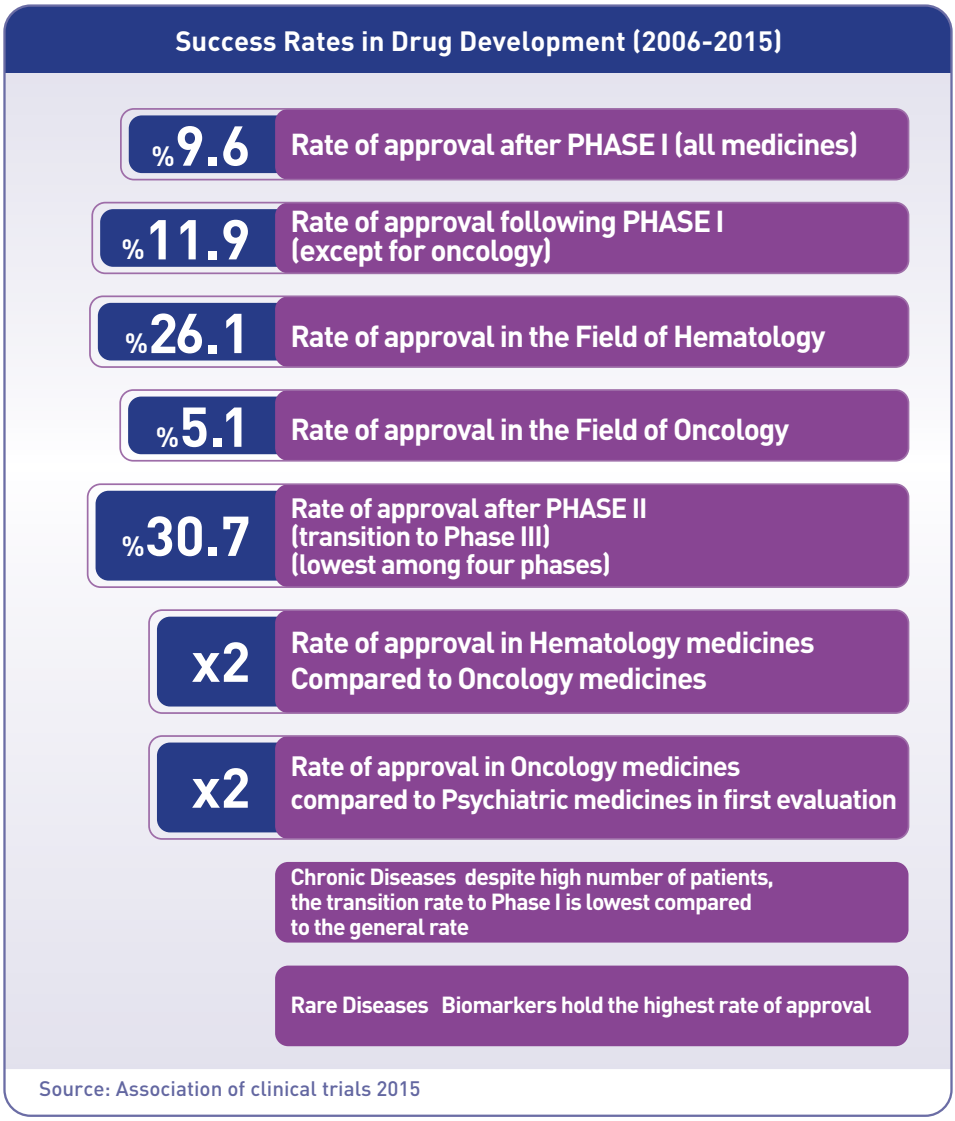
Source: PhRMA 2015 Profile

to nurture mostly basic research and discovery processes.

The infrastructure and projects intended for preclinical studies comprising laboratory and animal tests began to be brought up in recent years. The research infrastructure especially for the animal testing part of clinical trials is insufficient. The research infrastructure support provided by the Ministry of Development was re-arranged by a new law in 2014 and comprised the infrastructures intended for preclinical studies in its first call.

The ability to transfer the research outputs to the next phases in the value chain during the basic research process is important. It is not possible for the outcomes of all basic researches conducted to become directly useable and this also violates the nature of science. However, even if the outcomes of researches do or do not develop as expected, it is critical to ensure interaction between researches and unveil the those which complement each other. The interaction between the players in the same phase and different phases is important also for the coordination of investigators and their transfer to the next phase. From this respect, there are problems in Turkey regarding data infrastructure and the coordination of trials and players. This is the basis of the activation of the R&D ecosystem.

The pharmaceutical R&D in Turkey is not at the desired competitive level despite the current players and environment conditions. Within this scope, it is possible to utilize the current situation in Turkey in terms of the research infrastructure with education and human resources, regulatory environment and institutional infrastructure, financial resources and mechanisms, which constitute the main components of the ecosystem. Qualified human resources are among the key infrastructural components of the innovation ecosystem in all sectors. R&D and innovation activities, which may be regarded as the drivers of the transformation achieved by the pharmaceutical sector in Turkey on a global scale in recent years require that well-educated people, specialized in their own field and who may respond to the needs of the sector at each phase of the pharmaceutical value chain, are available in the labor market. One of the most important determinants of the quality of human resources in the fields of medicine and basic sciences which are required to make the pharmaceutical R&D ecosystem operational, is the quality of primary and secondary education in Turkey.



The performance of the education system in Turkey, which underwent many large and small changes in recent years, is unfortunately left behind compared to OECD countries and countries with a similar income level.

Considering the drug R&D ecosystem from the perspective of education and human capital, this emerges as a problematic area. Qualified human capital is a must in knowledge-intensive sectors with an increasing weight and the development of the R&D processes. Although Turkey avails of a human resource mass that may provide infrastructure for life sciences, a quality problem is noted both at the level of secondary education and university education in the current situation. With the decrease in the number of basic science programs and their quotas, it is probable that not only a quality problem but also a quantity problem will arise in the upcoming period. Therefore, it becomes important to make relevant changes in the design of the educational policies directed at the preparation of qualified human capital and in the education system and to solve the problems related to basic sciences in the high-technology transition period. It should be taken into account that the changes directed at education and human capital in the ecosystem are changes which may lead to results in the medium and long term in the ecosystem and that short-term mechanisms aimed at activating the ecosystem should certainly be elaborated.

COUNTRY	Per Patient Cost (USA = 1,00)	COUNTRY	Per Patient Cost (USA = 1,00)
USA	1,00	Spain	0,54
Norway	0,73	Italy	0,50
Ireland	0,71	Holland	0,49
Switzerland	0,69	**TURKEY**	**0,47**
UK	0,69	Portugal	0,46
Germany	0,66	France	0,45
Sweden	0,65	South Africa	0,41
Austria	0,63	Poland	0,40
Israel	0,62	Russia	0,39
Denmark	0,59	Romania	0,38
Belgium	0,58	Hungary	0,34
Finland	0,58	Ukraina	0,33
Kore	0,56	China	0,31

AIFD study, 2016

Research infrastructures constitute one of the most important components of the pharmaceutical R&D ecosystem. The number of research infrastructures in areas contributing to pharmaceutical R&D increased rapidly in Turkey with the research infrastructure support provided by the MoDev. One way to achieve the expected efficacy with such kind of research infrastructures is to ensure cooperation with the private sector. The cooperation of research infrastructures with the private sector and its utilization by the industry is limited to merely a few examples in Turkey and it is also observed that the cooperation of research centers with each other remains weak. It is seen that many research infrastructures repeat each other and that the absence of a monitoring mechanism makes it impossible to utilize the accumulation and accurately identify the needs.

One the other major problems is the lack of a data infrastructure to guide the research and consequently to enable the interaction of the outputs. The main reason for having infrastructures and projects which repeat each other and research projects which do not follow up on and complement each other is the absence of a data infrastructure. Furthermore, also the absence of a mechanism for tracking and evaluating the supports is another factor decreasing the efficacy. While there are many research infrastructures which repeat each other, the completion of the infrastructure directed at preclinical research, which was missing, was brought up only recently and this is still a major deficiency. The absence of an owner for the relevant processes and arrangements in addition to the deficiency of an infrastructure for preclinical studies constitutes a major problem. Having a technological infrastructure, know-how and a dynamic data infrastructure is crucial for providing an appropriate guidance and designating meaningful focal areas.

Major steps were taken in recent years in Turkey in the field of clinical trials which constitute the second fundamental phase of the pharmaceutical R&D value chain, starting with the structuring of relevant clinical trial regulations. While arrangements directed at the achievement of a more effectively operable system were structured, process became more rapid and were standardized as a consequence of this. Although problems relating to approval periods and standards are still brought up currently on an occasional basis, it is possible to say that major improvements were achieved. The hospital infrastructures where the clinical trials will be conducted are among the leading players of the ecosystem regarding clinical trials. Turkey avails of a significant hospital infrastructure and provides

a very convenient environment for clinical trials both in terms of patient population and infrastructure. Although genetic diversity as well as a young and large population make Turkey attractive for clinical trials, the number of clinical trials is below the expected level.

Turkey takes a share of only 7 per mille from the total clinical trials worldwide. Two percent of the trials conducted in Turkey are Phase I, 16 percent are Phase II and the remaining trials are Phase III and IV studies. In order for Turkey attract clinical trial investments, it is critical in terms of preferability that it offers more advantageous conditions compared to competing countries as with countries focusing on this area.

The 10th Development Plan aimed to make Turkey a global pharmaceutical R&D and production center in the long term with its "Action Plan for the Structural Transformation Program in Healthcare Industries", dated 2014. Within this scope, it is aimed to reach a competitive level in fields of medicines and medical devices, increase by 25% on an annual basis the share taken by Turkey from global clinical trial investments and the number of clinical trials conducted and to make investments reach 234 million dollars in 2018.

The members of the Association of Research-Based Pharmaceutical Companies (AIFD) perform a significant part of the clinical trial investments. Thus, AIFD members carry out clinical trials in 215 centers located in 54 provinces of Turkey in total. In 2016, AIFD members performed a total investment of 384 million dollars (115 million Euros) with 476 clinical trials. Twelve of the trials conducted are at Phase I.

AGENCY APPROVAL	Average Days (Arithmetic, Days)	Average Days (Median, Days)	Sponsorship (Arithmetic, Days)	Ethics Committee (Arithmetic, Days)	Agency (Arithmetic, Days)
First Application	133	105	15	16	103
Protocol Change	64	84	3	3	59

ETHICS COMMITTEE APPROVAL	Average Days (Arithmetic, Days)	Average Days (Median, Days)	Ethics Committee (Arithmetic, Days)	Sponsorship (Arithmetic, Days)
First Application	34	32	27	7
Protocol Change	34	28	27	6

ETHICS COMMITTEE APPROVAL (in years)	2015 Average Days (Arithmetic, Days)	2014 Average Days (Arithmetic, Days)	2013 Average Days (Arithmetic, Days)
First Application	34	34	43
Protocol Change	34	40	59

AIFD Clinical Trials Approval Survey, July 2016

However, it is believed that main areas in which Turkey needs to develop to achieve Globalization in Clinical Trials are as follows:

1- Development of new incentive mechanisms directed at the Clinical Trial investments; conduct of relevant legal arrangements for enabling Clinical Trials to benefit from R&D incentives,
2- Predictable and sustainable approval processes,
3- Elimination of the negative perception in the society about clinical trials,
4- Establishment of a system for the distribution of progress payments obtained from the trial,
5- Integration of the current developed national database systems (MEDULA) with the clinical trial.

SECTOR AND ECONOMY

The contribution of innovative companies to Turkish economy is not restricted with has been described so far and extends beyond R&D investments, foreign trade and employment. Research-based pharmaceutical companies offer therapeutic options intended for meeting the healthcare needs of Turkey and invest in humans who constitute the most important human capital of a country. Healthy individuals and a healthy society means a more productive manpower which constitutes a major component of a soundly growing economy and needs less acute and long-term treatment.

The pharmaceutical sector in Turkey reached a size amounting to 30 billion TL in 2015 and is ranked as the world's 16th largest country with this size. However, the share taken by Turkey from total exports remained low, reaching only 827 million dollars as of the end of 2016 according to the Turkish Statistics Institute.

Turkey prioritized the pharmaceutical industry in the correct manner and selected a sector that could help get out of the middle-income trap. Yet, we believe that the steps taken within the scope of localization and which may be defined as import substitution are not the policies required by Turkey, fall into conflict with the goal of global competitiveness and harm also the international investment policies of Turkey

Localization

The Tenth Development Plan, comprising the period 2014-2018, constitutes a major milestone in making our society reach a high welfare level in line with the 2023 goals of our country. Our country designated the strategic sectors to carry Turkey to a higher income level with a leap to be achieved in national income in line with this vision and our Government displayed a strong will on the path of structural transformation and reform with implementation-oriented plans, programs and action plans.

Within this framework, the pharmaceutical industry stands out as an industry which will contribute to the structural transformation of our economy, holds a high international competitive power, is based on R&D and innovation and avails of the capacity of selling goods and services to all global markets. Turkey aims to draw foreign direct investment (FDI) with higher added value from the global industry making an R&D investment of 141 billion dollars in 2014 figures.

However, the implementation of removing imported products from the reimbursement list, as indicated both in the 10th Development Plan and the 64th Government Action Plan, will not serve this goal of structural transformation and reform. However, it will only enable the continuation of the manufacturing structure and capacity aiming to meet the need of only generic product groups with a low added value in the current local market instead of global and regional markets. Therefore, the referred implementation does not serve the goal of making our country the center of production, management and procurement center in Eurasia upon increasing medium and high technology production upon developing the aimed local manufacturing technology within the framework of a political and economic vision.

Following "July 15", AIFD demonstrated its belief and commitment in Turkey once again, July 2016

The first phase of localization was expressed in the meeting held in January 2016 in Ankara, with the participation of 10 companies. The meeting, in which mandatory localization was requested, was followed by the communication of manufactured equivalent groups constituting the basis of localization, published by SGK in February. During the same period, firstly the information on the manufacturing capacity of companies was requested by TITCK and, consequently, information on unutilized manufacturing capacity (that can be used for toll manufacturing) outside the currently used capacity in manufacturing sites of companies with a pharmaceutical manufacturing facility was asked.

Yet, the problem is not that local manufacturing is not carried out in our country, but is the low level of quality in local production. The value and qualification of export goods of Turkey reveal the need for "High Technology- High Competitive Power – Capacity to Sell Goods and Services to Global Markets – Structural and Qualitative Transformation" of our manufacturing composition.

Our country has to transform its industrial manufacturing structure and specialize in high technology, branded production and trade of goods and services with high competitive power in order to achieve the goals and objectives set forth in the referred plans, programs and action plans with its 2023 vision and goals.

Positioned as one of the world's top 20 economies, Turkey designated its goal of getting 1% share from global trade with a strategic vision. In line with this strategic vision, our country is obliged to increase its exports and thus the goods and services sold to all global markets rather than meeting the local needs. Another important component of the same strategic vision stands out as the goal of becoming a "Regional Center". Becoming a "Regional Center" in terms of production, management and procurement brings along the implementation of a flexible foreign trade policy comprising liberal and "smart regulations" rather than protectionism in Turkey. "Being annexed to global supply and value chains" may be a key catalyst for achieving the referred increase in exports and being transformed into a regional center.

High-level strategic meeting, organized once a year with the participation of the representatives of the AIFD, European Federation of Pharmaceutical Industries and Associations (EFPIA) and Pharmaceutical Research and Manufacturers of America (PhRMA), was held in Ankara this year, September 2016

The basis of the foreign trade deficit and current deficit issues of our country lies in the industrial production structure with low technology, competitive power and added value and focused on meeting local needs. These issues cannot be solved based on short-term and palliative policies focused on "financial sustainability". Turkey's pharmaceutical industry does not avail of a structure which is independent from the general perspective we tried to depict above. The problem is not the inability to perform local production in our country, but that the technological level of the local production is not at a sufficient level and that high added value production is not performed.

Thus, there is need to achieve transformation to high added value production rather than supporting the current structure of local pharmaceutical production. Currently, the local production in our country meets nearly half of the market in value and seventy-five percent in units. Therefore, the problem is not the inability to perform local production, but the low quality of local production.

Delisting of import products from the reimbursement list will not enable the achievement of the results desired within the framework of the strategic vision outlined above. On the other hand, unfair competitive advantage will be achieved to the benefit of the current local production and this will serve the preservation of the production structure focused only on meeting local needs.

Furthermore, it is necessary to arrange support and incentives in a manner so as to make them oriented to all innovative and patented products, while designing and implementing them and to clearly define the relevant evaluation criteria. The achievement of the goals set forth by our country with the 2023 vision will be possible with policy tools at the level of smart regulations and transparent, competitive and sustainable solution proposals, rather than restriction/banning of imports and discussions of protectionism and interventionism.

Our messages in this direction were shared with the representatives of TITCK and SGK. Hence, the announcement on the "Localization Process" was published on March 4. It was indicated in the announcement that "The purpose of the work conducted within the framework of the action plan is not to remove import products from the scope of reimbursement, but to encourage local production within a predictable period." Moreover, the Commission on Transition from Imported to Manufactured Products was established with the participation of the representatives of the Medicines and Medical Devices Agency of Turkey (TITCK), Social Security Institution (SGK), Ministry of Development, Ministry of Finance, Ministry of Economy and Undersecretariat of Treasury and it was recorded that the whole process would be followed up by this commission. According to the scheduled timeline, it is planned to initiate the localization process of designated equivalent groups as of April 4, 2016 and relevant companies need to submit their commitments for transition to local production for their products until March 22, 2016. It is requested that the justifications on products for which no commitment is /can be made for localization by March 22, 2016.

This topic was presented as an important agenda item in the consultation meeting held between TITCK and the Sector three days later and it was indicated that the real purpose of this implementation was to enhance the production capacity in the country upon enabling the transition of imported products to local production.

When listing the steps to be taken within this scope in 10 items, it was indicated that the last item reading "the maintenance of reimbursement by SGK" would be applied reversely for products not providing any commitment and it was shared with the sector that the products of companies which failed to make an application or submit a justification would be removed from the reimbursement list.

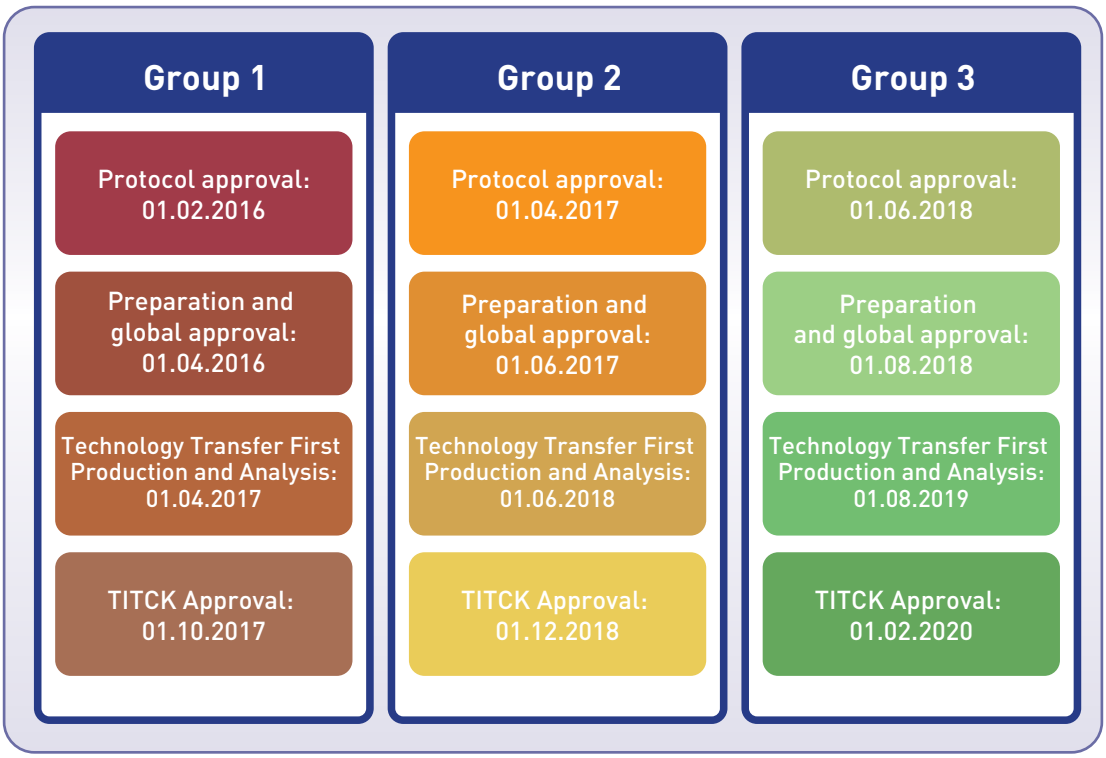
The steps taken/to be taken within this scope;

1. Identification of companies with a market share of manufactured products of above 50% and with the highest rate of imported product sales.
2. Conduct of meetings with companies and evaluations on a product basis.
3. Evaluation of the capacity status of the manufacturing sites in our country.
4. Preparation and announcement of the transition timeline (March 4, 2016).
5. Submission of applications by companies (March 22, 2016).
6. Evaluation of the Commitment Applications by the Commission on the Transition from Imported to Manufactured Products.
7. Evaluation of the status of products for which no commitment is made.
8. Submission of Variation applications for products for which commitment is made.
9. Issuance of variation (change in manufacturing site/localization) approvals by TITCK.
10. Continuation of reimbursement by SGK.

Steps taken/to be taken in the localization process of imported products, Consultation meeting between TITCK and the Sector, dated March 7, 2016

As the AIFD, we express in the most articulate manner that this erroneous message conveyed to international investors harms the business and investment environment. It is not an effective and fruitful method to punish private companies for obtaining more investments. A company may be producing some high value added and high technology products in Turkey while importing other products. Therefore, the imported products of a company which manufactures in Turkey and even has products which are exported to global markets will face the danger of being removed from the scope of reimbursement. This message will make it difficult for companies currently manufacturing in Turkey to adopt new investment decisions.

The transition calendar to last until 2020 in three phases was presented as follows in the referred meeting. Consequently, the 2nd and 3rd phases were merged and the deadline for the completion of the process was pulled back to the end of 2017.



Within the framework of the information provided to companies in April 29, it was reported that imported products with less than three local equivalents were excluded from the scope, that commitments indicating that the application for the transition to imported to manufactured status would be made maximum within 1 year to the Agency and that the requests and commitments other than these would be rejected. Companies received the first official letter regarding this topic at the end of December 2016.

Within this timeframe, it was shared with all decision-makers that this implementation does not comply with the acquis communautaire of the European Union (EU) and the international agreements to which Turkey is a party. Our country has obligations arising from the EU acquis within the scope of the ongoing full membership negotiations with the EU and the modernization of the Customs Union. Topics such as fair and free competition, predictability, transparency and "Freedom of Market Access" are important parameters of the "Presence of a well-operating free market economy" which is the prerequisite of the Single Market and full membership.

Clause 4, Article 3 in the General Agreement on Trade and Tariffs (GATT) requires imported products to be treated equally with similar local products regardless of the origin of the imported products. The policy for achieving an advantage in the registration, pricing and reimbursement conditions of the local products included into the action plan is regarded to be noncompliant with this agreement of which Turkey is a party.

Article 3 of the Trade-related Aspects of Intellectual Property (TRIPS) Agreement requires that no discrimination is made regarding the use of intellectual property rights between the citizens of that country and the citizens of member countries. It is believed that if the imported products covered by the localization policies included into the action plan are included into market access and reimbursement lists later or are excluded from the scope

of purchasing guarantee contracts, this will restrict the patent derived commercial gains of these products which is incompatible with the agreement.

It is believed that the revision of the registration procedures in a manner so as to provide advantages to locally manufactured products is regarded to be incompatible with clause 1, Article 2 in the Technical Barriers to Trade (TBT) Agreement.

It is stipulated in clause 1(a), Article 3 in the Subsidies and Countervailing Measures (SCM) Agreement that it is not possible to grant incentives based on the export performance. The implementation foreseeing the inclusion of the products manufactured for export purposes into the reimbursement list, as indicated in the transformation program, is regarded to be incompatible with SCM.

Multinational pharmaceutical companies operating in Turkey play a major role for the future of Turkey and we appreciate the efforts of decision-makers to pursue a reasonable path in the localization activities to be performed and to be understanding in terms of timing in the investment plans presented. Furthermore, as the achievement of the localization goal is expected, we hope that it is not preferred to remove the products which will not be localized from the reimbursement list. It should not be forgotten that this implementation may give

AIFD Survey prepared by using the IMS database, April 2016

rise to a negative impact for patients. Some large and known brands will disappear from the market due to this implementation and millions of people will be obliged to change the medicines they had been using for years.

Official letters began to be sent to companies in the last days of 2016 and information was provided on the plans presented. According to the reference made to the decisions of the Healthcare Services Pricing Commission (SHFK), it was indicated that the decision to remove rejected products at the end of 1 year would be taken by the Reimbursement Commission of SGK. Registration variation applications are expected to be submitted within one year as of the announcement of the decision for accepted products.

However, based on the principle of reciprocity, also the possibility of other countries to resort to similar implementations should be taken into account. International trade is shaped on the basis of mutual interest (Reciprocity). Banning imports may lead also other countries to adopt similar measures and thus may prevent the products of Turkish manufacturers from entering certain markets.

As shared in the International Convention of Pharmaceuticals and Pharmacies (IVEK) BIO workshop held in December, the second phase of localization began with the direct talks carried out with companies in January 2017. In the second phase planned to be completed within one year, the share of locally manufactured products, previously designated as 30% and above, was dropped to 10% and the condition of having at least three local manufacturers was reduced to two.

Due to the reasons mentioned above, we believe, as the AIFD, that the "mandatory localization" or "forcing localization with the threat of being removed from the scope of reimbursement" is not an appropriate implementation for Turkey and harms the perception about the business and investment environment in Turkey from an international perspective.

Modernization of the Customs Union

The Ankara Agreement, signed in 1963 between the European Economic Community (EEC) and Turkey, envisaged the establishment of the Customs Union during the transition phase, prior to the full membership of Turkey. Based on the decision adopted in the EU Accession Partnership Council meeting held on March 6, 1995, Turkey established a Customs Union with the EU as of 1996. The fact that 21 years elapsed since this process, foreseen to be temporary, and the obligations nevertheless undertaken by Turkey, which is not included into the decision-making mechanisms of the EU as it is not a full member, due to the trade agreements signed by the EU with third parties, brought on the agenda the need for the Customs Union to be revised.

After the inclusion of the update of the 20-year agreement into the decisions of the EU-Turkey summits held on November 29, 2015 and March 18, 2016, the European Commission requested authority from the European Council on December 22, 2016 to renew the Customs Union agreement between Turkey and the EU.

Thus, the Association of Research-Based Pharmaceutical Companies (AIFD) established its first contacts with the representatives of the Directorate General for Trade of the European Commission in the meeting held in January in Ankara. Information was provided on three prioritized topics of the pharmaceutical sector.

Pharmaceutical Production and Export Ecosystem Report, TEPAV, September 2016

Turkey signed the Association Council Decision with No. 1/95, establishing the Customs Union with the EU in 1995. It is observed that Turkey's imports from the EU increased, while a notable increase occurred in exports in the period 2002-2007, following Customs Union. Yet, it may not be stated that the Customs Union functions adequately in ensuring a trade balance with the EU. Therefore, the topic of updating the Decision of the Customs Union came up and a memorandum of understanding was signed on May 11, 2015 for making amendments on the agreement.

It was agreed to make changes on three topics in the Customs Union Decision. The first topic of agreement is to include the sectors of agriculture, services and public procurement into the scope of the Customs Union. The second topic on which agreement is reached is to grant the right to move freely for Customs Union goods in road transportation and to remove cuts. This will enable the reduction of transportation costs as well as a more rapid delivery. The third topic is that Turkey may become a direct party to the agreements to be signed by the EU with third countries.

The second and third topics of agreement are steps of particular concern also for the pharmaceutical sector. In this sense, it will be possible to shorten the transportation period with the reduction in bureaucratic transactions. Distribution is a topic greatly emphasized by the pharmaceutical sector. The medicines within the distribution process need to be preserved under certain standards. The obstacles to be encountered in distribution may be reflected negatively on medicines. At this point, the free movement of products within the scope of the Customs Union eliminates this danger. Having Turkey as a party to the agreements to be signed by the EU with third countries in order to do business expands Turkey's trade route. This item also brings up the topic of Turkey's being indirectly party of TTIP to be signed with the EU and the US.

Manufacturing and Exports

The Pharmaceutical Production and Export Ecosystem Report, prepared by TEPAV with the support of the AIFD, was launched to the public in Ankara on September 26, 2016.

The meeting held with the participation of the authorities of TEPAV and the AIFD and the representatives of the public and private sectors and foreign investments for the presentation of this new report of a complementary nature for the Pharmaceutical R&D Ecosystem Roadmap Report published in 2015, was attended also by the representatives of MoH, MoE, MoDeV, SSI, Treasury and TUBITAK.

During the event, which began with the opening speeches of TEPAV's Executive Director, Güven Sak and AIFD's Chairman of the Board of Directors, Dr. Mete Hüsemoğlu and continued with the presentation delivered by TEPAV's Program Director for Innovation Studies, Selin Arslanhan Memiş, the roadmap for advanced technology was discussed in detail with focus group meetings held in the afternoon.

The launch of the Pharmaceutical Production and Export Ecosystem Report, prepared by TEPAV with the support of the AIFD, September 26, 2016

TEPAV's Executive Director Güven Sak, who referred to the importance of the event in terms of the new growth strategy of Turkey, continued as follows: "In order to achieve the technological leap much needed currently, Turkey needs to transfer new technologies and widespread these technologies throughout the country. The pharmaceutical sector is among the leading sectors to accelerate this process. We are delighted to find the opportunity to discuss by convening with the regulators from the public side and local and foreign companies from the private sector side the roadmap we have outlined for the achievement of the leap to advanced technology in this meeting. We need to complete our preparations and take action as soon as possible for this technology transfer which constitutes one of the main topics of the global agenda. At this point, we need select the technology and not the sector and designate concrete mechanisms to ensure the flow of this project." Güven Sak concluded his words by recording the following: "It is highly important to provide a suitable investment

environment for foreign investors regarding the transfer of new technologies to Turkey".

AIFD's Chairman of the Board of Directors, Dr. Mete Hüsemoğlu recorded the following: "One of the most important missions of our Association is to contribute to the generation of effective solutions for the health issues in Turkey. I may state, as the representative of 38 global pharmaceutical companies, that it is crucial that innovation and innovative medicines provide a positive contribution to human life. We had published 'Turkey's Pharmaceutical Sector Vision 2023' report in 2012 in relation with this mission upon taking into account also the priorities of the public. We continue to share on a continuous basis our strategy and policy proposals on the development of the Turkish pharmaceutical sector. This study holds a great importance regarding this purpose. There is need for local and foreign investments in order to achieve the desired development in the pharmaceutical sector. We need to establish the public and private sector cooperation in the most efficient manner so as to support these investments and provide the most suitable environment. We believe that this meeting and the report, the findings of which will be shared today, will provide guidance for the concrete steps to be taken in this direction. Two most important steps to be taken on this path are to generate policies together and to trust each other."

Following the opening speeches, TEPAV's Program Director for Innovation Studies, Selin Arslanhan Memiş presented the framework of the Pharmaceutical Product and Export Ecosystem report and emphasized 6 key points standing out in the report:

1. Turkish economy underwent a major transformation in the last three decades along with the structural factors as well as the change occurred in the production and export composition. The greatest source of growth for the economy during this process was the productivity growth with the rural-to-urban migration. Today, the urbanization rate in Turkey is close to 75%. It is no longer possible to preserve the productivity growth in order to make Turkey grow with the manpower movement from the agriculture to services and industry. It is necessary to grow with the productivity growths within the sector from now on and not with the productivity growth coming with migration. Now, Turkey needs a new growth strategy aiming to achieve productivity growth with the sector via a structural transformation. What required to be done in 1980 to make the per capita income amounting to US$ 1.500 to US$ 10,000 and what needs to be done in order to make increase it from US$ 10,000 to US$ 25,000 are not the same. Despite July 15 coup attempt, the state of emergency applied consequently and recently increasing problems both across the world and in Turkey, now Turkey should return to its economy agenda and be focused on the sustainable development and growth strategy formulated with structural reforms.

2. The relationship between growth and sustainability in recent years begins to turn positive through new technologies. While carbon emissions increased with the increase in industrialization previously, new technologies enable productivity growth simultaneously in different sectors and reduce carbon emissions currently.
This provides an opportunity to facilitate the transfer and diffusion of new technologies to developing countries such as Turkey. Also the global agenda is shaped around this topic. In order not to be excluded from these discussions and to benefit from this opportunity, Turkey should designate its focus as soon as possible, establish its structural reform agenda and designate a new development and growth strategy in line with global trends. Turkish economy made transition from a low-technology structure to a medium-technology structure in the last 30 years. But, the share of advanced technology still remains too low. What needs to be done now is to designate an

industrial policy focusing on the transfer and diffusion of new technologies to enhance quality in traditional sectors and increase advanced technology exports.

3. The world is undergoing a technological transformation. The way business is done, from industry to services, agriculture to energy, is reshaped with the impact of new technologies. It is possible to observe the technological reflections of scientific developments and the difference generated by these reflections in the manufacturing processes every single day. Furthermore, the focal point of this change is the provision of solutions to the global problems impacting increasingly sustainability. Sustainability issues have been positioned at the center of the global agenda in the last few years and became the problem of all countries. Along with the definition of the 'Sustainable Development Goals', also the agreement of countries on this topic were revealed. Both as a party to this agreement and from the perspective of its development and economic policy, Turkey should do new things about this topic at this point. One of the most important factors to enhance productivity within the sector is technological renewal. As a requirement of this renewal, the most important component of Turkey's sustainable growth and development strategy is to achieve a technological leap and accelerate the share of advanced technology in production and exports. Technological renewal carries importance for economic growth with productivity growth within the sector and the achievement of "Sustainable Development Goals" with the transformation to come with the impact of new technologies.

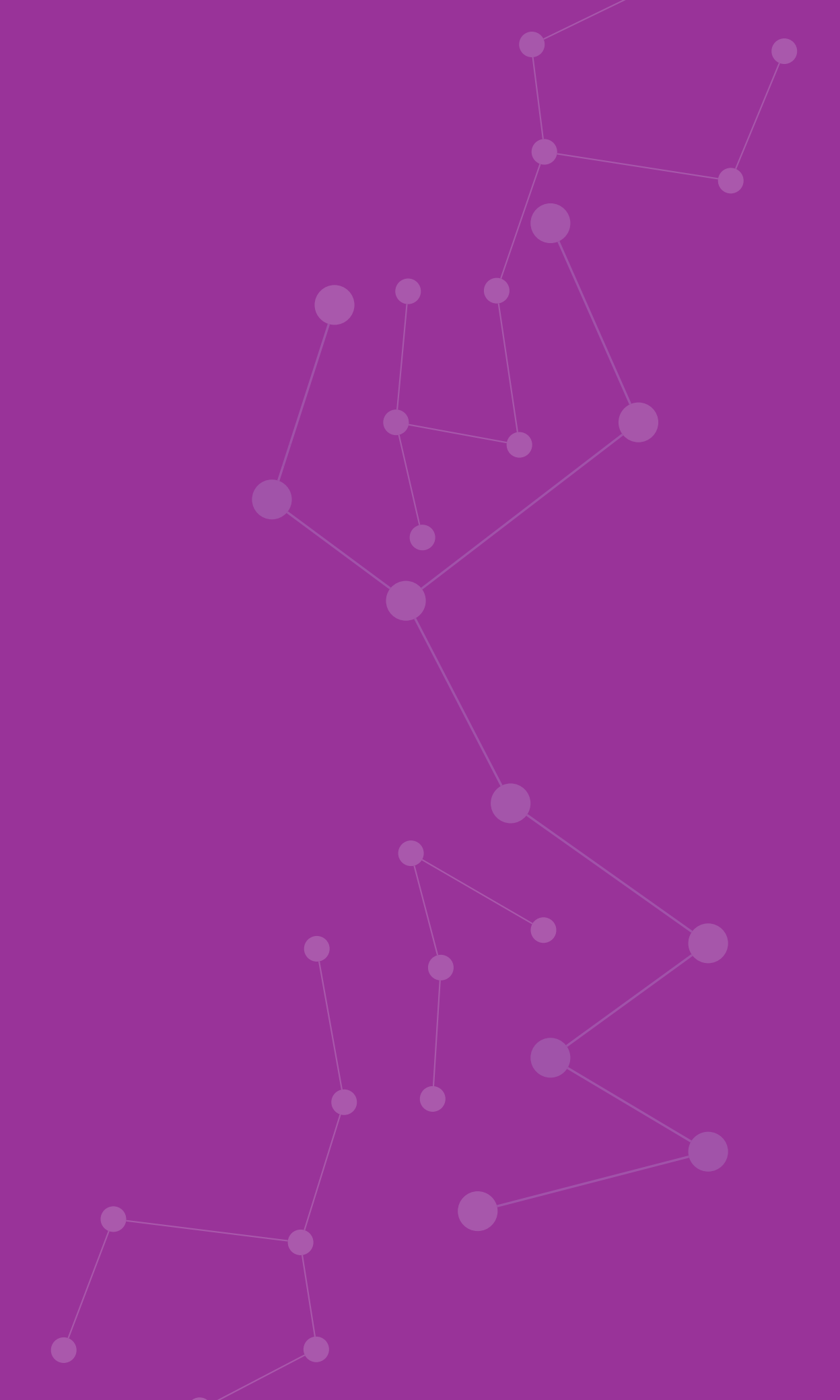
4. The technological priorities of Turkey need to be aligned with those of the world. The technological transformation the world has been undergoing in recent years derives mainly from three technology platforms, namely, Biotechnology, Nanotechnology and Information & Communication Technology (ICT). The difference in these new technologies is that they avail of the potential to transform multiple sectors simultaneously. This is also what Turkey needs to achieve a rapid leap. The most important component of this new growth strategy should be to accelerate this technological leap. The greatest need is technology-focused industrial policy which can make a selection in order to accelerate the technology transfer and enhance advanced technology exports. The objective of this report is to present a roadmap for contributing to the design of a new growth strategy and an industrial policy focused on technological renewal. The report complements previously published Pharmaceutical R&D Ecosystem Roadmap Report. This time, the following stages of the value chain, namely, production and exports were examined closer. Due to the potential carried in terms of the increase in advanced technology production and exports and the opportunities provided for transfer of biotechnology, which is one of the three new technologies, the pharmaceutical sector is a candidate for becoming one of the prominent sectors of the new growth strategy. In addition to the importance it carries for the technological leap in exports as a sector with advanced technology, what distinguishes the pharmaceutical sector from the other sectors with advanced technology is that it is qualified as a sector that may accelerate the transfer of biotechnology and its widespread in Turkey.

5. The key for the pharmaceutical sector to benefit from this potential is an effectively operating ecosystem design and a competitive investment environment. The increase of investments both in the local and foreign private sector is very important for technological transformation. Therefore, the institutional infrastructure needs to be taken up again for the new growth strategy. The steps to be taken in reform areas such as jurisdiction, incentives and the education system and an investment environment where economic predictability is enhanced are even more important today. Although the investment criteria and impact levels differ in terms of the investments to be made in different phases of the value chain, the basic joint criterion for all investments is

consistency. Having predictable, transparent and consistent legal arrangements of the country in which investments are to be made are placed at the top of prioritized conditions. In addition to the improvement of horizontal environment conditions with structural reforms, there is need for tools accelerating transition and concrete projects. When it is necessary to make operable the mechanism intended for a growth and development strategy focused on technological renewal, ecosystem components which we may classify as horizontal and vertical are unveiled. Horizontal components are the environment conditions required for operating this technology-focused mechanism. It is necessary to ensure relevant environment conditions in order to achieve a leap with new technologies. Whereas, vertical components are arrangements and tools necessitating to be selective among sectors and differentiation and which accelerate technology transfer and diffusion.

6. Very important steps were taken in recent years from this respect via public policies. Furthermore, new arrangements were introduced in order to improve the investment environment in recent years. Being included into the 10th Development Plan and Transformation Programs, the establishment of the Biotechnology Strategy and the effective operation of the Healthcare Industries Steering Committee are steps which constitute a positive framework for the future. But, what needs to be done now is to prioritize the reform steps around a specific field of focus and also take privileged steps for accelerating sectors. Contributing to making the actions defined by public programs in the transition process to advanced technology operational is also among the key objectives of this report. This roadmap, defined by setting off from deficiencies and exemplary models, aims to serve as a catalyst and support the current steps by covering the whole value chain together with the previous R&D Ecosystem Report and comprises concrete steps accelerating the process. While completing the improvements required in the medium and long term in the production and export ecosystem for the transition to advanced technology, there is also need for accelerating steps to make the ecosystem become operational. This study presents a prioritized roadmap comprising the accelerating tools intended for the short and medium term activation of the production and export ecosystem of the pharmaceutical sector which may be positioned as an accelerating sector for achieving a technological leap.

The launch of the Pharmaceutical Production and Export Ecosystem Report, prepared by TEPAV with the support of the AIFD, September 26, 2016



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