Research Article

Hacettepe University Journal of the Faculty of Pharmacy
Volume 39 / Number 2 / July 2019 / pp. 65-80

Evaluation of R&D Activities and The Perspectives of The Participants of Pharmaceutical Companies on R&D In Turkey

Türkiye'de İlaç Ar-Ge Faliyetlerini ve İlaç Firması Katılımcılarının İlaç Ar-Ge Üzerine Görüşlerini Değerlendirmek

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Received date : 26.12.2019
Accepted date : 08.04.2020

ÖZET

Araştırma, ilaç firmalarının Ar-Ge faaliyetlerini, ulusal ve uluslararası ilaç firmalarının Ar-Ge, veya Medikal & Klinik Araştırma ve Pazarlama Departmanlarında çalışanların Ar-Ge ile ilgili görüşlerini değerlendirmek amacıyla yapılmıştır. Bu araştırmada evren olarak Araştırmacı İlaç Firmaları Derneği (AIFD), Türkiye İlaç Endüstrisi İşverenler Sendikası (İEİS) ve Türkiye İlaç Sanayi Derneği üyesi olan ilaç firmaları arasından belli kriterleri karşılayan 81 ilaç firması tüm evren olarak saptanmıştır Ar-Ge ile ilgili çok sayıda konuyu kapsayacak 50 soruluk bir anket oluşturuldu. Anket geribildirimlere bağlı olarak geliştirildikten sonra online uygulamaya açılmıştır. Araştırmaya hedeflenen 81 ilaç firma içinden 51 firma katılmış ve katılım oranı % 63 olmuştur. Araştırmaya her firmadan 2 bölümün katılması hedeflenmiştir. Online ankete firmanın Ar-Ge bölümünden bir uzman, eğer firmanın Ar-Ge bölümü yoksa Medikal veya Klinik Araştırma bölümünden bir sorumlu katılmıştır. Araştırmaya ikinci grup olarak Pazarlama bölümü belirlenmiştir ve araştırmaya bu bölümden de bir pazarlama sorumlusu katılmıştır. Her firmadan iki kişinin katılması beklenen araştırmaya 51 firmadan toplam 96 kişi katılmıştır. Ancak bazı pazarlama profesyonelleri çeşitli nedenlerden dolayı bu online ankete katılamamıştır. Verilerin istatiksel analizi için SPSS 22 programı kullanılmıştır. Araştırmanın sonuçları Türkiye ilaç sektöründe Ar-Ge faaliyetlerinin ve yatırımlarının yetersiz olduğunu işaret etmiştir. Ulusal ilaç firma katılımcıları bu faaliyetlerin yetersizliği ile ilgili olarak "Vizyon eksikliği", "Finans-man yetersizliği", "Teşvik yetersizliği" ve "Devlet-sanayi iş birliği eksikliği" seçeneklerini önem derecesine göre daha yüksek değerlendirirken, uluslararası ilaç firma katılımcıları da bu nedenlere ilave olarak "Patent sorunu" ile "Alt yapı yetersizliğini" de önemli nedenler arasında saymışlardır. Hem ulusal hem de uluslararası ilaç firma katılımcıları yabancı ilaç firmalarının Türkiye'ye Ar-Ge yatırımı yapmama nedenlerini önem derecesine göre değerlendirdiklerinde, önemli nedenler olarak "Türkiye'yi stratejik olarak tercih etmeme" ve "Fiyatlandırma politikaları" seçilmiştir. Uluslararası ilaç firma katılımcıları "Patent" ve Devlet desteği eksikliğini" de diğer önemli nedenler olarak eklemişlerdir. Uluslararası ilaç firmaları Türkiye'de yalnız klinik araştırmalar yapmaktadır.

Anahtar Kelimeler: İlaç Ar-Ge, biyoteknoloji, ulusal ilaç firmaları, uluslararası ilaç firmaları, klinik çalışmalar

ABSTRACT

The purpose of this study is to evaluate both R&D activities and investments of pharmaceutical companies and the views of of participants on R&D.

For this research, pharmaceutical companies who were the members of Association of Research based Pharmaceutical Companies (AIFD), Pharmaceutical Manufacturers Association of Turkey (IEIS) and Pharmaceutical Industry Association of Turkey (TISD) and who met the screening criteria were identified as universe. In order to address many issues in the study, the questionnaire included 50 questions. After validating the questions, the survey was rolled out online. Fifty one pharmaceutical companies participated in this research with a 63% participation rate. Two departments from each company were included in this online survey. If the company has an R&D department, one R&D specialist, if not, one specialist from Medical or Clinical Research department participated. The marketing department was selected as a second group for the study and one professional from this department completed the online survey. Ninety six respondents completed the survey with the expectations of two professionals from each company. For the statistical analysis of the data, SPSS 22 program was used. Results indicate that R&D activities as well as investments in Turkish pharmaceutical industry were not sufficient. The major reasons for the insufficiency were the "Lack of vision", "Lack of financial incentives", and "Lack of government and industry cooperation" reported by the participants of both companies. Additionally, "Patent problem and Intellectual Property Rights", and "Lack of infrastructure" were also chosen by the respondents of international pharmaceutical companies. The important reasons for international pharmaceutical companies for not establishing their R&D centers in Turkey were "Not to choose Turkey strategically" and "Pricing policies". Additionally, "Patent problem" and "Lack of Government support" were selected as other important reasons by the participants of international companies. International pharmaceutical companies as part of their R&D efforts only conduct clinical trials in Turkey.

Keywords: Pharmaceutical R&D, biotechnology, national pharmaceutical companies, international pharmaceutical companies, clinical studies

1. Introduction

Numerous researchers reported R&D as an important factor supporting the competitiveness of the company as well as its impact on competitiveness of nation. The most R&D intensive industry in the world is the pharmaceutical industry (1). Drug development comprises all the activities involved in transforming a compound from a drug candidate (the end-product of the discovery phase) to a product approved for marketing by the appropriate regulatory authorities. Drug development is the process of bringing a new drug molecule into the clinical practice (2). R&D in the pharmaceutical industry involves several phases from basic research identifying a new molecule in the laboratory and clinical research proving the effectiveness and safety of the molecule for humans to the approval of the medicine. R&D also helps to improve the drug safety and to develop new formulations and combinations of existing products (1). It takes 10 to 15 years on average for a potentially promising candidate drug that is identified and optimized, to pass through the entire R&D process and to be approved. Among the potential drug candidates, only 12% enter the clinical trials and ultimately approved by the FDA. The average cost to develop a new medicine is estimated as $2.6 billion dollars, including the cost of failures (3).

Performing R&D in the pharmaceutical sector, the sector that allocates the most resources to R&D in the world, is crucial for sustainable economic growth with its spread of effects (4). R&D plays a very important role in economic development of countries. R&D is an indicator of the level of development of countries and is also measured by the size of resources allocated by countries (5). There is a competition between developed and developing countries when it comes to R&D. Unfortunately developing countries typically lag behind in global competition because they do not allocate sufficient resources for R&D or do not fully understand the importance of R&D (5). Today, innovative performance is a crucial factor in determining competitiveness and national progress. Moreover, innovation is important to help address global challenges, such as climate changes and sustainable development (6). In the 21st century, strategies based on knowledge and innovation have become one of the basic conditions of competitiveness both at country and company level (6). The main

actors of the innovation ecosystem are universities, research centers, public institutions, companies and entrepreneurs. Innovation is the result of the interaction of these actors with each other under appropriate environmental conditions. The environmental conditions that feed this ecosystem are financial resources, incentive mechanisms, regulations, education, human resources and investment factors (4).

Pharmaceutical R&D expenditures increased by 241% from 92.1 million TL in 2010 to 314.1 million TL in 2017 (7).The rate of use of biotechnological drugs in the world has exceeded 20% and this rate continues to increase. A similar situation is observed in Turkey. Biotechnological drugs reached 5.5 billion TL, with a 17.6% market share, in the prescription market in Turkey in 2018 (7).

According to the 2018 Global Innovation Index report, 8 European countries are ranked within top 10, Turkey is ranked the 50th amongst 126 countries (8). In the Global Competitiveness Index report 2017 -2018 Turkey is ranked the 54 amongst 137 countries (9). On Feb 28, 2019 a total of 1.133 accredited R&D centers with 56.974 staff are reported in Turkey, about 28% of which are the Pharmaceutical R&D centers (10).

2. Materials and Methods

In this study, the quantitative research method was utilized and the data was collected via online survey. Out of 81 pharmaceutical companies who were the members of Association of Research Based Pharmaceutical Companies (AIFD), Pharmaceutical Manufacturers Association of Turkey (IEIS) and Pharmaceutical Industry Association of Turkey (TISD) 51 companies were recruited to complete the survey by the time research started. Eighty one pharmaceutical companies who met the screening criteria out of all of members of the non-profit organizations whose names were found on official web pages of the above non- profit organizations were identified as universe. Total of ninety-six respondents participated in this online research. Fifty five respondents of 96 were from international pharmaceutical companies and 41 from national pharmaceutical companies. Online survey was conducted with R&D or Medical & Clinical Research and Marketing departments. Forty five respondents represented marketing, 22 represented R&D, and 29 respondents represented Medical & Clinical Research. Throughout the analysis of this study R&D and Medical & Clinical Research departments were gathered under one group and Marketing was considered as a second group. Figure 1 il-

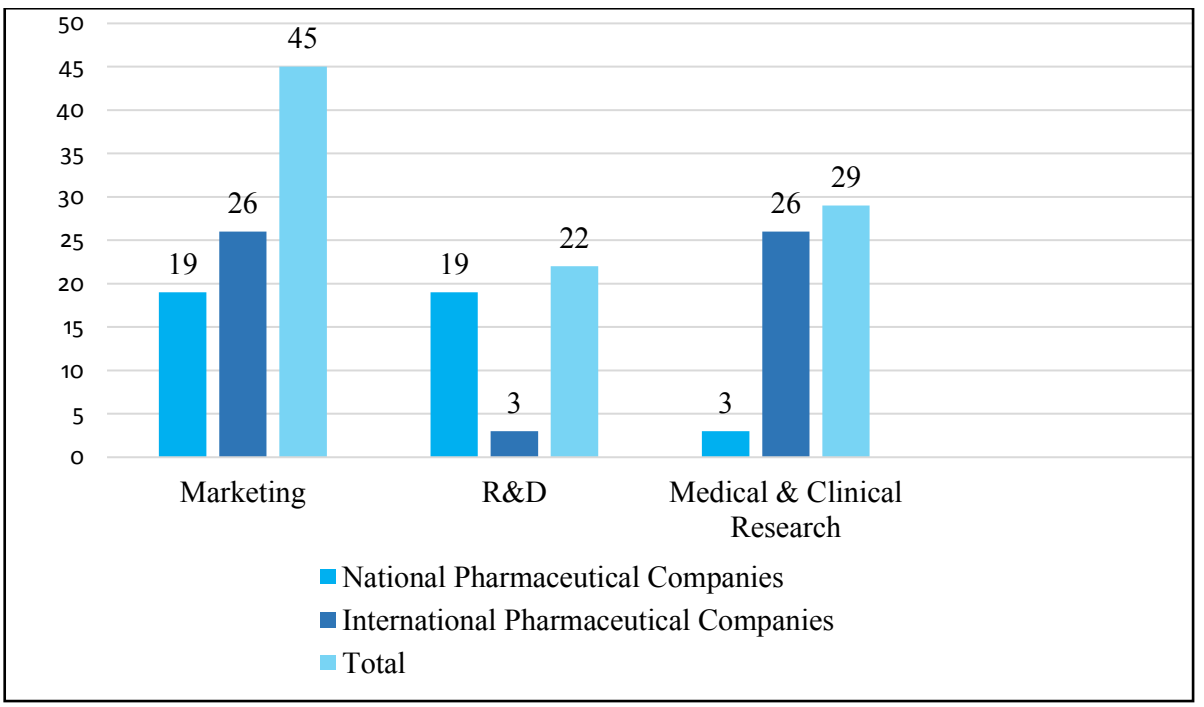

Figure 1: Respondent analysis by company and department

ISSN: 2458 - 8806

lustrates the breakdown of participants by company and functional area.

Nineteen (46.34%) respondents of national pharmaceutical companies represented Marketing, 19 (46.34%) represented R&D, and 3 represented (7.3%) Medical & Clinical Research. Twenty six (47.27%) respondents of international pharmaceutical companies represented Marketing, 3 (5%) represented R&D, while 26 (47.27%) participated from Medical & Clinical Research Departments.

Respondents were analyzed by the type of company, department, years of experience and profession in the Table 1.

Among the 96 respondents, 41 respondents were from national and 55 respondents were from international pharmaceutical companies. If we have a look at the attendance ratio, 47% werefrom marketing, 23% were from R&D, and 30% were from medical /clinical departments. In terms of experience, over 60% of the respondents selected the range between 11- 20 years. Only 4% chose 31 years and above. With respect to profession, 28% of the participants were medical doctors and 17.71% were engineers, 13.54% were pharmacists, 12.50% were chemists and 12.50 % were from the field of business administration & marketing, and 9.38% were gathered in biology. The rest were economists and others.

Completion of online survey with 96 respondents took 7 months throughout 2017. The respondents who wanted to fill out the survey had to approve the consent form by clicking the button for approval. Online survey included a total of 50 questions and the vast majority of the survey questions were close-ended. SPSS 22 program was used for statistical analysis of the data.

Ethical approval regarding this study was granted by the Ethical Committee of Okan University on February 2, 2017.

Table 1: Descriptive statistics of respondents

Variables		n	%
Company Type	National	41	42.71
	International	55	57.29
Department	Marketing	45	46.88
	R&D	22	22.92
	Medical and Clinical Research	29	30.21
Years of Experience	1-10 years	26	27.08
	11-20 years	60	62.50
	21-30 years	6	6.25
	31 years and above	4	4.17
Profession	Medical Doctor	27	28.13
	Engineer	17	17.71
	Pharmacist	13	13.54
	Chemist	12	12.50
	Biologist	9	9.38
	Business Administration / Marketing	12	12.50
	Economists	3	3.13
	Others	3	3.13

n: number of participants

The purpose of the research was explained at the beginning of the online survey. After respondents read the details of the research, they clicked on the consent button to proceed on survey.

3. Results and Discussion

Respondents from national and international companies evaluated R&D activities and investments in Turkish pharmaceutical sector as "Insufficient" (Figure 2 and Figure 3, in respectively).

In terms of evaluation of R&D activities 68 (71%) respondents found R&D activities in Turkish pharmaceutical market as "Not sufficient" or "Not sufficient at all". Only 1 respondent found R&D activities "Sufficient", and 16 (16.6 %) respondents found "Neither sufficient or nor insufficient" (Figure 2).

The reasons for the insufficiency of R&D efforts in the Turkish pharmaceutical sector were listed in the Table 2.

Most of the respondents from national pharmaceutical companies chose "Lack of funding", "Lack of vision", "Lack of incentives", "Lack of government and industry cooperation" and "Lack of qualified personnel" as important factors for the insufficiency of R&D efforts excluding foreign partnership necessity; the respondents from international companies selected all reasons as important factors excluding foreign partnership requirement. There is a statistically significant difference between national and international pharmaceutical companies, in respect to lack of funding and lack of incentives. In terms of importance, respondents from national pharmaceutical companies rated lack of funding and lack of incentives higher than the respondents of international pharmaceutical companies.

Figure 3 illustrates the reactions of respondents of international and national pharmaceutical companies to R&D investments in the Turkish pharmaceutical sector. In terms of evaluation of R&D investments in the Turkish pharmaceutical sector total of 72 (75%) respondents found R&D investments either "Not sufficient" or "Not sufficient at all". 43 (78%) respondents from international pharmaceutical companies found sector "Not sufficient" or "Not sufficient at all", 29 (78%) respondents from national pharmaceutical companies found industry "Not sufficient"

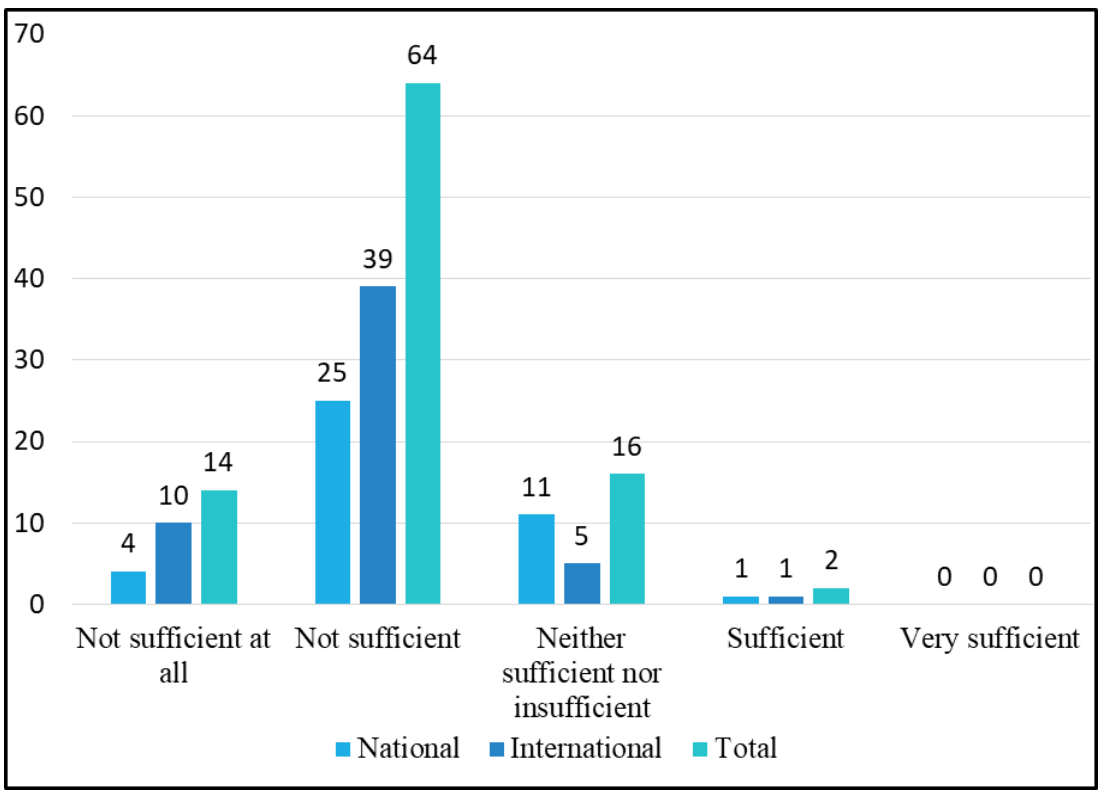

Figure 2: Evaluation of R&D activities in the Turkish pharmaceutical sector

ISSN: 2458 - 8806

Table 2: Reasons for the insufficiency of R&D Activities in Turkey

	National		International		Mann Whitney U	
	Median	$\bar{X}$±SD	Median	$\bar{X}$±SD	Z	p
Lack of Vision	4	4.02±0.96	4	4.16±0.88	-0.695	0.487
Lack of Funding	4	4.32±0.72	4	3.93±0.88	-2.159	0.031*
Lack of Qualified Personnel	4	3.78±1.15	4	3.65±1.25	-0.397	0.692
Lack of Incentives		4.12±0.84	4	3.75±0.99	-1.925	0.050*
Patent Problems (IPR)	4	3.37±1.26	4	3.76±1.09	-1.566	0.117
Lack of Technology	3	3.37±1.18	4	3.58±0.99	-0.958	0.338
Lack of Infrastructure	3	3.39±1.20	4	3.76±1.04	-1.608	0.108
Lack of Government and Industry Cooperation	4	4.02±0.79	4	4.00±0.92	-0.159	0.873
Foreign Partnership Requirement	3	2.71±1.35	3	3.07±1.03	-1.508	0.132

z: Mann Whitney U test Mean SD: Standard deviation *p<0,05

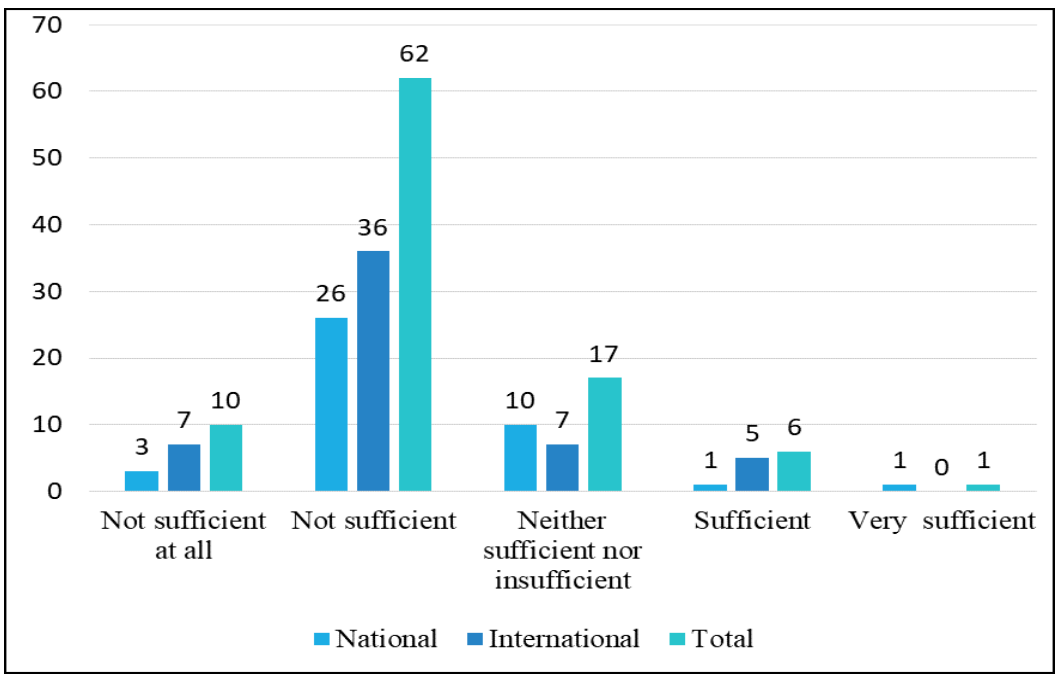

Figure 3: Evaluation of R&D investments in the Turkish pharmaceutical sector

or "Not sufficient at all". Only 2 respondents from international companies and 5 respondents from national pharmaceutical companies rated R&D activities in the Turkish pharmaceutical sector either "Sufficient" or "Very sufficient".

With regard to R&D potential of the Turkish Pharmaceutical industry, 28 (51%) respondents from international pharmaceutical companies evaluated the industry "Not sufficient" or "Not sufficient at all", 20 (36%) respondents from international companies found industry potential "Sufficient" or Not Sufficient at all; 18 (44%) respondents from national phar-

maceutical companies found R&D potential of Turkish pharmaceutical industry "Sufficient" or "Very sufficient". 9 (22%) respondents from national pharmaceutical companies and 7 (17%) respondents from international companies found R&D potential of the industry "Neither sufficient nor insufficient". No statistically significant difference is observed between national and international pharmaceutical companies.

In terms of productivity of the industry 47 (85%) respondents from international pharmaceutical companies evaluated the productivity of industry "Not sufficient" or "Not sufficient at all". Only 2 (4%) respondents found industry productivity "Sufficient", 6 (11%) respondents from international pharmaceutical companies found industry productivity "Neither sufficient nor insufficient"; twenty one respondents (51%) from national pharmaceutical companies found the industry productivity "Not sufficient" or "Not sufficient at all". Only 3 respondents (7%) evaluated industry productivity as "Sufficient", while 17 respondents (41%) found industry productivity "Neither sufficient nor insufficient". With respect to productivity of pharmaceutical industry there is a statistically significant difference between international and national pharmaceutical companies.

Forty three (78%) respondents from international companies evaluated the impact of R&D investment on the competitiveness of the Turkish pharmaceutical industry either "Very effective" or "Effective", only 7 respondents found R&D investment on the competitiveness of the Turkish pharmaceutical industry "Not effective" or "Not effective at all". Thirty six (88%) respondents from national companies found the effectiveness of R&D either "Effective" or "Very effective."

There is a statistically significant difference between the respondents of national and international pharmaceutical companies (Table 3). More respondents from national companies rated impact of R&D investment on the competitiveness of the Turkish pharmaceutical industry "Very effective".

Figure 4 illustrates the percent allocated to R&D from gross revenues of pharmaceutical companies. While national pharmaceutical companies reported allocating 1-19% of their gross revenues to R&D, international pharmaceutical companies reported allocating 11- 21% and above. Nearly 71% of participants of international pharmaceutical companies mentioned that they were either satisfied or very satisfied with the percent their companies allocated to R&D, while this rate was only 26% for the participants of national pharmaceutical companies.

Respondents from international and national pharmaceutical companies evaluated the level of R&D investment of international pharmaceutical companies in Turkey (Table 4). When it comes to reasons regarding why international pharmaceutical companies are not investing in R&D in Turkey, "Pricing policies" statement was chosen a very important reason by the respondents of international pharmaceutical companies and an important reason by the respondents of national pharmaceutical companies. "Not choosing Turkey strategically" was an important reason for both pharmaceutical companies. In addition to the reasons mentioned above, the participants of international pharmaceutical companies chose "Lack of government support", Lack of patent/ IPR" and "Lack of infrastructure" as other important reasons of international pharmaceutical companies for not investing in R&D in Turkey. When it comes

Table 3: Assessment of impact of R&D investment on the competitiveness of the Turkish pharmaceutical industry

	National		International		Total		p
	n	%	n	%	n	%	
Not effective at all	1	2.44	3	5.45	4	4.17	p=0.017*
Not effective	1	2.44	4	7.27	5	5.21	
Neither effective nor ineffective	3	7.32	5	9.09	8	8.33	
Effective	14	34.15	27	49.09	41	42.71	
Very effective	22	53.66	16	29.09	38	39.58	

chi square test n: number of participants $p<0.05$*

ISSN: 2458 - 8806

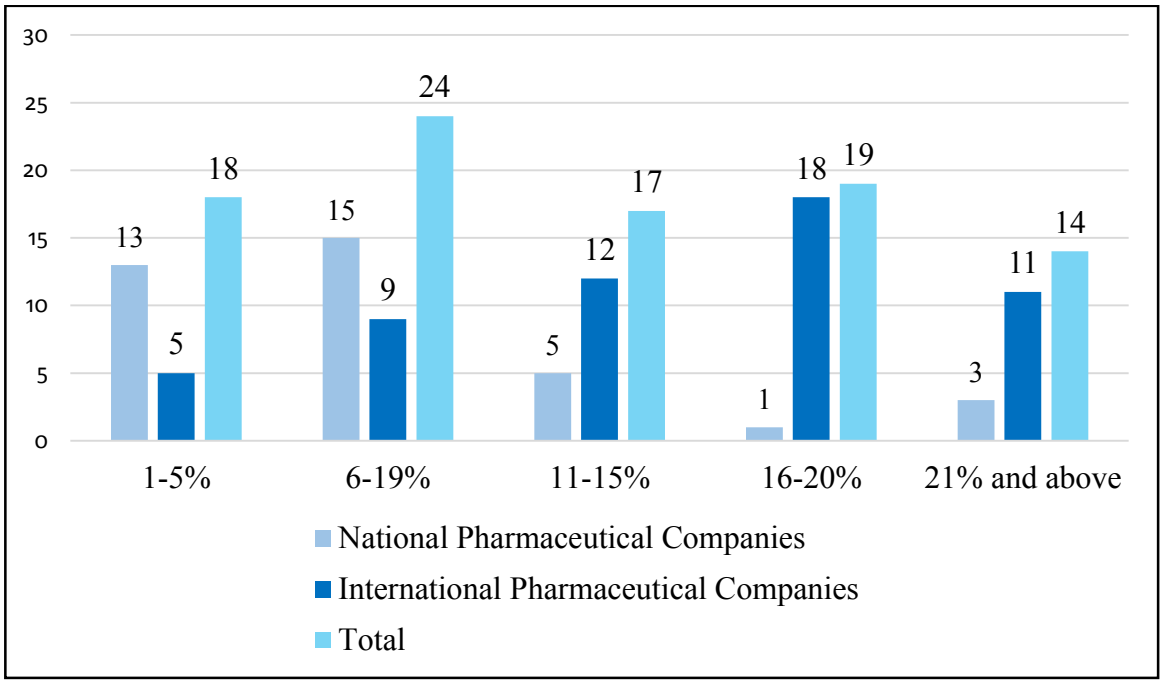

Figure 4: Percent allocated to R&D from gross revenues of pharmaceutical companies

Table 4: Evaluation of the reasons of international pharmaceutical companies for not investing in Turkey

	National		International		Mann Whitney U	
	Median	$\bar{X}$±SD	Median	$\bar{X}$±SD	z	p
Lack of qualified personnel	3	2.98±1.44	3	2.91±1.21	-0 197	0.844
Lack of infrastructure	3	3.15±1.42	4	3.40±1.21	-0.866	0.386
Lack of technology	3	2.85±1.20	3	2.98±1.19	-0.629	0.530
Not choosing Turkey strategically	4	3.68±1.27	4	4.22±0.83	-1.943	0.048*
Patent/IPR	3	3.29±1.17	4	3.87±1.17	-2.524	0.012*
Lack of government support (tax, exempt)	3	3.44±1.34	4	3.69±1.00	-0.729	0.466
Pricing policies	4	4.10±1.11	5	4.35±0.89	-1.039	0.299

z: Mann Whitney U Test $\bar{X}$: Mean SD: Standard deviation *p<0.05

to "Not choosing Turkey strategically" and "Patent /IPR", there is a statistically significant difference between national and international pharmaceutical companies. Respondents from international pharmaceutical companies rated these reasons higher than the respondents of national pharmaceutical companies. When the participants were asked to assess their own companies' pipeline, 73% of participants of national pharmaceutical companies reported developing branded generics, 49% reported new formulations, 56% reported developing innovative medicines, 39% reported developing biotechnology

products, and 46 % reported developing biosimilars. Among the participants of international pharmaceutical companies 84% respondents mentioned developing innovative medicines, 58% mentioned biotechnology products, about half mentioned new formulations and 18% mentioned biosimilars. Concerning innovative medicines and branded generics, there is a statistically significant difference between national and international pharmaceutical companies. As expected, higher number of respondents from international companies chose innovative medicines compared to the respondents of national pharmaceutical companies. Regarding branded generics higher number of respondents of national pharmaceutical companies selected branded generics compared to international pharmaceutical companies.

When the respondents were asked to evaluate their own companies' R&D potential and efficiency, 21 (59.46%) respondents from national companies rated their own company's R&D potential "Sufficient" only, 7 (19%) respondents found the company R&D potential "Not sufficient" and 8 (21%) respondents found the company "Neither sufficient nor insufficient". Forty one (71%) respondents from international pharmaceutical companies evaluated their own company's R&D potential "Sufficient or "Very sufficient". While 8 (14.5%) respondents found the company R&D potential "Insufficient", 6 (11%) respondents found R&D potential of their own company's R&D potential "Neither sufficient nor insufficient". From an R&D potential point of view there is a statistically significant difference ($p<0.05$) between international and national pharmaceutical companies. Regarding R&D efficiency of the company, 18 (49%) respondents from national pharmaceutical companies found R&D efficiency of their own company "Sufficient or "Very sufficient". 13 (35%) respondents (35%) found it "Neither sufficient nor insufficient, while 6 (16%) respondents found R&D efficiency "Sufficient". However, Schuhmacher, Gassmann and Hinder indicated that some pharmaceutical companies analyzed the saving potential of R&D and then they cut their units to increase their R&D efficiencies in their article, namely Changing R&D Models in Research-based Pharmaceutical Companies (9).

International pharmaceutical companies reported only performing certain clinical trials as part of their R&D efforts in Turkey. Breakdown of clinical trials by company is shown in Figure 5. More than 50% of the participants from international pharmaceutical companies reported conducting Phase III and Phase IV in Turkey. Only a few respondents mentioned Phase I and Phase II. While 65% of the participants

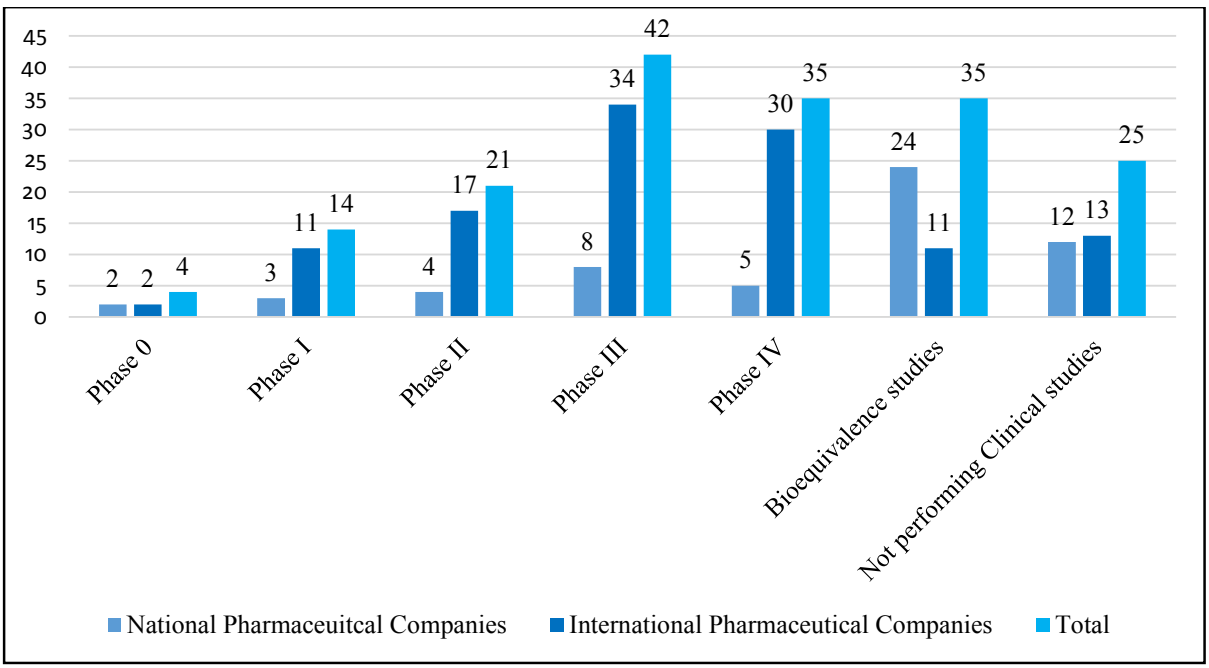

Figure 5: Type of clinical studies conducted by pharmaceutical companies in Turkey

ISSN: 2458 - 8806

of national pharmaceutical companies reported conducting bioequivalence studies, 32% of the participants reported for not conducting any clinical study in Turkey.

Respondents were asked if their companies established any collaboration with universities, 27 (73%) respondents from national pharmaceutical companies chose "Yes" while 3 (8%) respondents selected "No" , 7 (18.9%) respondents chose "Don't know"; while 35 (63.6%) respondents from international pharmaceutical companies chose "Yes", 9 (16.4%) respondents said "No" and 11 (20%) respondents chose "Don't know" options. (Table 5).

Respondents who stated their companies were collaborating with universities and institutes provided the names of universities /institutes in Table 6. Universities/institutes were grouped by region in the same table. Most respondents (n= 57) collaborated with universities in Marmara region and it was followed by the Anatolia region with 27 respondents (Table 6).

Pharmaceutical companies have continued to use their own equity as R&D resources, 31(84%) respondents of national pharmaceutical companies reported receiving support from TUBITAK / TEYDEP. Foreign partnership was reported as the least important R&D source for national pharmaceutical companies while 7 (12.7%) respondents from international companies chose "TUBİTAK/TEYDEP", and only 6 (11%) chose "Foreign partnership."

Respondents of International pharmaceutical companies reported having several R&D centers all over the world. These reported R&D centers were located in the USA (31 centers), Europe (26) and Asia (21), LA (4) and Israel (2). Respondents from national pharmaceutical companies reported having one R&D center in Turkey, mainly in the Marmara Region.

Summary of the evaluation of R&D functional area against other areas in the company from value-added and sustainability point of views was shown in Table 7. Respondents of national and international pharmaceutical companies also evaluated the impact of R&D on the competitiveness of any pharmaceutical company. With respect to value –added impact of R&D and contribution of R&D to sustainability of the companies the participants of international pharmaceutical companies rated these statements significantly higher than the participants of national pharmaceutical companies. However, when the impact of R&D on competitiveness of any company was asked, the participants of national pharmaceutical companies rated R&D significantly higher than the participants of international pharmaceutical companies Table 7.

Respondents were asked to evaluate the following statements on a scale from 1 to 5 (1 means strongly disagree and 5 means strongly agree). Respondents reactions to those statements were shown in Table 8. Respondents from national and international pharmaceutical companies were asked to rate the statements listed above. "R&D is necessary for company differentiation", "Company should have R&D policy and strategies" and "R&D performing company develops know-how" were rated higher than other statements listed in Table 8. Only the "Foreign partnership is essential for performing R&D" statement was rated lower than all other statements. In order to see the differences between national and international pharmaceutical companies based on the statements listed in Table 8, the level of R&D importance was calculated by using a formula in Table 9.

Table 5: Cooperation between pharmaceutical companies and universities

	National		International	
Responses of pharmaceutical companies	**n**	**%**	**n**	**%**
Yes	27	73	35	63.6
No	3	8.1	9	16.4
Don't know	7	18.9	11	20.0
Total	37	100	55	100

n: number of participants

Table 6: Universities or institutes pharmaceutical companies are collaborating with by region

REGIONS	n	UNIVERSİTIES /INSTITUTES
Marmara Region	54	Istanbul University Faculty of Pharmacy, Koç University, Bosphorus University, Yıldız Technical University, Marmara University, Sabancı University, Kocaeli University, Duzce University, Uludağ University, Onsekiz Mart University, Medipol University, Yeditepe University, Bezmi Alem University, Namık Kemal University, Acıbadem University
Egean Region	6	Ege University (Ar-GEFAR), 9 Eylül University
Anatolia Region	27	Hacettepe University, Gazi University, Middle East Technical University, Ankara University, Bilkent University
Black Sea Region	3	19 Mayıs University
East and South East Anatolia	5	Erciyes University, Gaziantep University
International Universities/ Institutes	7	Harvard, University, Copengahen University, Leuven Catholic University, Boston's Children Hospital, Telethon Institute of Genetics and Medicine
Local Institutes	14	Gebze High Techology Institute, TÜBİTAK, TÜBİTAK MAM

n: number of participants

Table 7: Evaluation of R&D importance

	National	International	Mann Whitney U Test (p)
Value -Added Impact of R&D	3.88±0.84	4.33±0.7	0.050*
Contribution of R&D to Sustainability	4.30± 0.79	4.61±0.66	0.039*
Impact of R&D on Competitiveness	4.76±0.49	4.44±0.63	0.045*

z: Mann Whitney U test $\bar{X}$: Mean standard deviation *$p<0.05$

In terms of importance level of R&D, there is no statistically significant difference between the responses of national and international pharmaceutical companies.

The findings of this online survey supported that R&D and technology have an impact on the competitiveness of pharmaceutical companies and industry. The research article on "Technology and competitiveness" written by Bayraktutan and Bidirdi had mentioned that companies who designed future technologies, developed the strategy for technology, conducted R&D and gave importance to technology development would gain a competitive advantage in international markets. (10).

Bunnage stated that it is essential for pharmaceutical companies and their scientists to become better connected with the external research environment and to develop a more extended network of partnerships and genuine collaborations with academia, in his commentary article on "Getting Pharmaceutical R&D Back on Target published in Nature Chemical Biology Journal (11). In this research, the respondents from both national and international pharmaceutical companies mentioned that their companies were collaborating with universities for R&D efforts. In the same article Bunnage commented on the productivity challenge of large pharmaceutical companies based on lack of new molecular entities (NMEs) developed relative to R&D spending each year. Moreover, respondents from international pharmaceutical companies had found their companies productivity sufficient.

The respondents from both national and international pharmaceutical companies were asked to evaluate each of the following factors related to R&D on the competitiveness of the company, the ratings were listed in Table 10. Considering median numbers in the table "High technology", "Know-how transfer", and "Patent" factors were rated higher by the respondents of international pharmaceutical companies than

ISSN: 2458 - 8806

Table 8: Evaluation of various statements related to R&D

	Strongly disagree		Disagree		Neither agree nor disagree		Agree		Strongly agree		
	n	%	n	%	n	%	n	%	n	%	Mean±Sd
R&D is necessary for differentiation of the company	1	1.0	1	1.0	1	1.0	19	19.8	74	77.1	4.71±0.65
R&D performing company becomes a market leader	1	1.0	3	3.1	34	35.4	32	33.3	26	27.1	3.82±0.91
R&D performing company gains an advantage for sustainability	-	-	-	-	6	6.3	41	42.7	49	51.0	4.45±0.61
R&D performing company gains competitive advantage locally and globally	-	-	-	-	4	4.2	49	51.0	43	44.8	4.41±0.57
R&D performing company gains technological advantages	-	-	-	-	6	6.3	47	49.0	43	44.8	4.39±0.60
R&D performing company develops know-how	-	-	-	-	4	4.2	29	30.2	63	65.6	4.61±0.57
R&D performing company gains economic/financial advantages.	2	2.1	2	2.1	21	21.9	34	35.4	37	38.5	4.06±0.94
Employment quality increases in R&D performing company	-	-	3	3.1	12	12.5	47	49.0	34	35.4	4.17±0.76
R&D performing company's market value increases	-	-	-	-	8	8.3	37	38.5	51	53.1	4.45±0.65
R&D performing company contributes to economy.	-	-	-	-	7	7.3	37	38.5	52	54.2	4.47±0.63
Investment in biotechnology/ biosimilar is extremely important.	2	2.1	2	2.1	11	11.5	37	38.5	44	45.8	4.24±0.89
Companies should have an R&D policy and strategies.	-	-	-	-	1	1.0	30	31.3	65	67.7	4.67±0.50
There is a need for strong patent law for R&D investments	2	2.1	1	1.0	6	6.3	34	35.4	53	55.2	4.41±0.83
IPR should be strengthened for R&D investment	1	1.0	3	3.1	8	8.3	34	35.4	50	52.1	4.34±0.84
Foreign partnership is essential for performing R&D	19	19.8	24	25.0	30	31.3	16	16.7	7	7.3	2.67±1.18
Government incentives should be raised for R&D.	-	-	2	2.1	9	9.4	29	30.2	56	58.3	4.45±0.75

the respondents of national companies whereas only "New formulation" and "Productivity" factors were rated higher by the respondents of national pharmaceutical companies in comparison to international pharmaceutical companies. When it comes to "Know-how transfer", "Foreign partnership" and "Patent" factors, there is a statistically significant difference between national and international companies. The respondents of international pharmaceutical companies rated these last three factors mentioned above higher than the respondents of national pharmaceutical companies.

Study Hypotheses

Hypotheses were tested based on the opinions of the respondents from national and international pharmaceutical companies (Table 11).

H1: There is a strong positive correlation between the competency level of R&D activities and the views of participants on R&D incentives in the Turkish Pharmaceutical Industry.

Table 9: R&D importance level

	National		International		Student t Test		
	Median	$\bar{X}$±SD	Median	$\bar{X}$±SD	t	sd	P
Importance level of R&D	82.8	82.05±9.96	79.7	81.48±8.27	0.307	94	0.759

P>0.05

Table 10: Evaluation of each factor related to R&D on the competitiveness of the company

	National		International		Mann Whitney U Test	
	Median	$\bar{X}$±SD	Median	$\bar{X}$±SD	Z	P
High technology	4	4.34±0.69	5	4.55±0.72	-1.726	0.084
Know-How Transfer	4	4.17±0.83	5	4.55±0.54	-2.213	0.027*
Qualified technical personnel	4	4.29±0.81	4	4.42±0.63	-0.503	0.615
New formulation	5	4.46±0.60	4	4.16±0.76	-1.897	0.058
New molecule	5	4.56±0.74	5	4.76±0.47	-1.253	0.210
Biologics	5	4.37±0.73	5	4.42±0.71	-0.350	0.727
Biosimilars	4	4.29±0.81	4	3.96±0.88	-1.896	0.058
OTC	3	3.07±1.03	3	3.24±1.07	-0.683	0.495
Production	4	4.20±0.81	4	4.02±0.85	-1.086	0.277
Foreign partnership	3	2.80±1.23	4	3.51±1.00	-3.001	0.003**
Export	4	4.22±0.82	4	4.02±0.95	-0.957	0.338
Productivity	5	4.46±0.64	4	4.16±0.86	-1.722	0.085
Innovation culture	5	4.54±0.60	5	4.64±0.59	-0.976	0.329
National clinical studies	4	3.93±0.88	4	4.22±0.71	-1.611	0.107
Patent	4	4.24±0.66	5	4.51±0.63	-2.050	0.040*
Pricing	5	4.41±0.92	5	4.58±0.60	-0.388	0.698

ISSN: 2458 - 8806

Table 11: Study Hypotheses

		Turkish Pharmaceutical Sector Competency Level of R&D Activities	
		National (n=41)	**International (n=55)**
Evaluation of the views of the participants on R&D Incentives in the Turkish Pharmaceutical Sector (H1)	r	0.663	0.474
	p	0.001**	0.001**
Evaluation of R&D Potential of Turkish Pharmaceutical Sector (H2)	r	0.035	0.115
	p	0.828	0.402
Evaluation of R&D Efficiency of Turkish Pharmaceutical Sector (H3)	r	0.522	0.367
	p	0.001**	0.006**
Evaluation of level of R&D Investment of International Pharmaceutical ompanies in Turkey (H4)	r	0.104	0.286
	p	0.516	0.034*

r=Spearman's correlation test n: number participants *p<0.05 **p<0.01

	National Pharmaceutical Companies n=41	International Pharmaceutical Companies n=55
r	0.663	0.474
p	0.001**	0.001**

n: number participants P<0.01

H2: There is no positive correlation between R&D activities and R&D potential of Turkish Pharmaceutical Sector for both national and international pharmaceutical companies.

	National Pharmaceutical Companies n=41	International Pharmaceutical Companies n=55
r	0.035	0.115
p	0.828	0.402

n: number participants p>0.05

H3: There is a strong positive correlation between R&D activities and R&D efficiency of Turkish Pharmaceutical Sector.

	National Pharmaceutical Companies n=41	International Pharmaceutical Companies n=55
r	0.522	0.367
p	0.01**	0.006**

n: number participants P<0.01

H4: There is a positive correlation between R&D activities and the level of investment of international pharmaceutical companies in Turkey for the respondents of international companies. No positive correlation was obtained for the respondents of national pharmaceutical companies.

	National Pharmaceutical Companies n=41	International Pharmaceutical Companies n=55
r	0.04	0.286
p	0.516	0.034*

n: number participants P<0.05

4. Conclusion

Although there are major differences between national and international pharmaceutical companies in terms of R&D expenditures, number of R&D centers, types of product development, and global competitiveness, only a few important differences in the views of respondents towards R&D are identified. Most national pharmaceutical companies have been directing their R&D efforts toward branded generics and biosimilars instead of concentrating on innovative medicines. Therefore, the importance of R&D function/department to the company from value-added and sustainability point of views was evaluated lower than other functional areas by the respondents of national pharmaceutical companies. International pharmaceutical companies do not have R&D centers in Turkey and they are mainly conducting clinical studies in Turkey. For this reason, the major focus of international companies is on clinical development of pharmaceutical R&D in Turkey. A few international pharmaceutical companies are in the process of collaborating with Turkish universities for basic research and drug development.

In general, the importance of foreign partnership requirement for R&D efforts was rated lower in comparison to many other factors contributing to R&D by the respondents from national pharmaceutical companies. However, we all know that Turkey needs a high -tech transfer from developed countries through partnerships.

Although participants either work for international or national pharmaceutical companies, they mostly exhibit similar views towards R&D based on the responses showing significant differences. We even don't see a major difference when we look at the study hypotheses. A reason for this is that because the respondents are from the same country and culture. In order to foster the R&D culture in the company, R&D policy and strategies should be developed and disseminated companywide and throughout affiliates.

5. Limitations

There isn't a similar type of research conducted with pharmaceutical companies regarding drug R&D activities both nationally and internationally. Several pharmaceutical companies did not want to participate in this survey although knowing that it was an academic research. It was a quite challenge to reach a significant number of respondents from both national and international pharmaceutical companies for the statistical analyses. As a further step, a research focusing on a few areas of R&D instead of covering many different topics should be conducted.

6. Acknowledgement

We would like to thank the respondents from national and international pharmaceutical companies for participating in this study and sharing their views with us. The authors do not have any conflict of interest (financial/non-financial) with subject, and there is not any financial or personal relationship that may bias the work.

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