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Original Article

DRUG DATA EXCLUSIVITY IN TURKEY FROM THE PERSPECTIVE OF PHARMACEUTICAL COMPANIES

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Abstract

The purpose of this study is to determine conceptions and/or disagreements of local and foreign drug companies in Turkey about data exclusivity – the most controversial issue between generic and original pharmaceutical companies all over the world – during the implementation period of the new drug approval regulation. The material of this study is a questionnaire to be replied by members of Turkish Pharmaceutical Manufacturers Association. According to the shared opinion of local and foreign companies (59.4%), generic drug companies will attach importance to research and development activities in the long term. Data exclusivity will be able to encourage the generic companies to produce original drugs. Although Turkish local companies are not able to invent orjginal drugs for today, 60% of local companies that replied the questionnaire survey think that data exclusivity has an encouraging role on research and development. 66.7% of local companies that replied the questionnaire think that equivalent drug policy will not go on with data exclusivity. However, 94.1% of foreign drug companies think that equivalent drug policies will go on with data exclusivity. Although data exclusivity can cause negative effects such as decreasing in the market size of local pharmaceutical companies, in majority both of local and foreign companies perceive the data exclusivity as a necessary and beneficial change. Because replies of questionnaire state that data exclusivity has positive effects in the long term such as increasing on investments of foreign pharmaceutical companies in Turkey, encouraging the local companies for research and development activities.

Key Words: *Data Exclusivity, Data Protection, TRIPS Agreement*

İlaç Firmalarının Bakışından Türkiye'de İlaçta Veri İmtiyazı

Bu çalışmanın amacı, Türkiye'de faaliyet gösteren yerli ve yabancı ilaç firmalarının bütün dünyada olduğu gibi Türkiye'de de büyük tartışmalara neden olan veri imtiyazı konusunun ülke mevzuatına yerleştirilme aşamasındaki görüşlerini ve görüş ayrılıklarını belirterek, yapılan mevzuat değişikliği sırasında Türk İlaç Endüstrisi'nin veri imtiyazı konusuna nasıl baktığını saptamaktır. Çalışmanın materyalini Türkiye'de faaliyet gösteren ve İlaç Endüstrisi İşverenler Sendikası'na üye olan yerli ve yabancı ilaç firmaları ile yapılan anket formları oluşturmaktadır. Yerli ve yabancı firmaların ortak görüşüne göre (%59,4), halihazırda genellikle jenerik üretim yapan firmalar uzun dönemde araştırma ve geliştirme faaliyetlerine önem verecek, veri imtiyazı uygulaması orijinal ilaç üretimine bir teşvik olabilecektir. Türkiye'de yerli sanayide orijinal ilaç üretimi bugünkü şartlarda mümkün değildir. Buna rağmen anket çalışmasına katılan yerli firmalar da %60 oranında veri imtiyazının araştırmayı teşvik edici olduğu yönünde görüş bildirmiştir. Çalışmaya katılan yerli firmaların %66,7'si veri imtiyazı uygulamasıyla birlikte devletin ucuz ilaç alım politikasının devam etmeyeceği görüşünü belirtmişlerdir. Yabancı ilaç firmalarının %94,1'i bu politikanın devam edeceği görüşünü belirtmişlerdir. Bu çalışmada veri imtiyazının, yerli ilaç endüstrisinin ürünlerinin sayısının azalması, ilaç pazarının küçüleceği gibi olumsuz etkilerine rağmen orijinal ilaç üreticilerinin Türkiye'deki yatırımlarını artırmaları, yeni ilaçların Türkiye piyasasına girişinin hızlı olması ve yerli ilaç endüstrisinin araştırma ve geliştirmeye teşvik edilmesi gibi uzun vadeli olumlu etkilerinin olması sebebiyle çalışmaya katılan ilaç firmalarının çoğunluğu tarafından gerekli ve yararlı bir değişim olarak algılandığı görüşüne varılmıştır.

Anahtar Kelimeler: *Veri İmtiyazı, Veri Koruması, TRIPS Anlaşması*

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INTRODUCTION

In order to market a new drug in Turkey, it is required to get drug product approval from the Ministry of Health according to the "Legislation for Medicinal and Pharmaceutical Products" and the "Regulation for Human Medicinal Products Certification" (1).

To get drug certificate for an original product, originator applicant should present all of the pharmaceutical (toxicological, pharmacological and clinical) data about the new drug. Generic drug companies can make abridged applications to get market approval for their products. To make an abridged application, generic applicants must only demonstrate that their product is bioequivalent to the original drug. They don't need to repeat the clinical safety and efficacy trials performed by the originator company (2). They can refer to the originator's data in order to make an abridged application. In many countries, health authorities don't allow the use of originator's data as a reference for abridged applications by generic companies for a period (usually 6 or 10 years) after the original product gets approval. This application is known as data exclusivity (3).

Data exclusivity was first noticed by the community with health care organizations' revision of their reimbursement policies to favor cheaper products in 2002 (4).

The Turkish Government is eager to qualify and become a full member of European Union without facing significant increases in health care costs and without significantly disrupting the competitive position of local generic manufacturers. Therefore, Turkey subscribed to apply the data exclusivity with TRIPS (Trade Related Intellectual Property Rights) and Customs Union agreements (5).

Data exclusivity caused some discussions between local and foreign drug companies until the publication of "Human Medicinal Products Licensing Regulation" in 19th of January, 2005. According to this regulation, data exclusivity is limited with patent period and is not retrospective (2).

There are two fundamental regulations about data exclusivity in Turkey. These are; "Decree Law No. 551 on the Protection of Patent Rights" dated 1995 and "Human Medicinal Products Approving Regulation" dated 2005.

Third paragraph of 83rd article of Decree-Law No. 551 on the Protection of Patent Rights in Force (from June 27, 1995) is as follows:

"Patent authority keeps the information and test results secret. These results and information are required for the approval of manufacturing and marketing human, veterinary or herbal medicines which are applied for a patent. Production and recording of this information which is not disclosed to the public by patent owner, needs considerable expense and effort. The authority will take the necessary cautions to prevent the inappropriate use of the information (6)."

When the paragraph is analyzed, we can see clearly that protecting the "secret information" is obligatory in Turkey, but the paragraph doesn't mention about the duration for protecting the "secret information" (7).

The recent regulation about data exclusivity in Turkey – Human Medicinal Products Licensing Regulation – was published on 25705 numbered Official Newspaper on 19th January, 2005. Ninth article of this regulation is about abridged applications and it determines these the duration of data exclusivity and the relationship between the patent duration and the data exclusivity duration. According to the regulation, data exclusivity starts 1st of January, 2005 and is limited with patent duration. Data exclusivity is not retrospective except the original drugs which their generics have not been approved between the dates of 1.1.2001 and 1.1.2005.

During the implementation period of this regulation, data exclusivity caused a lot of arguments in Turkish Pharmaceutical Industry. Local companies wrote disaster scenarios and foreign companies were the opposite side by defending data exclusivity as a very beneficial basic intellectual property right for all. There are financial reports printed by pharmaceutical companies about possible effects of data exclusivity before publication of the regulation. When these financial reports have been printed, there was not a clear regulation about how data exclusivity would be applied. Therefore, variables of financial analysis (such as beginning of year and duration of data exclusivity and relationship with patent period) were estimated. So the losses of generic companies, the benefits of original companies and additional government expenditure are all estimated amounts in these financial reports.

Nonetheless, there are not many objective studies on the opinions of pharmaceutical companies about data exclusivity.

The purpose of this study is to determine conceptions and/or disagreements of local and foreign drug companies in Turkey about data exclusivity – the most controversial issue between generic and original pharmaceutical companies all over the world – during the implementation period of the new drug licensing regulation.

EXPERIMENTAL

The material of this study is a questionnaire replied by members of Turkish Pharmaceutical Manufacturers' Association (by 2002, this association had 53 local and foreign members) (8). Each questionnaire includes 17 questions and all were filled out by regulatory affairs managers, business development coordinators and corporate affairs directors of the companies by face-to-face interviews, mails and e-mails. Data gained from the questionnaire is collected between June, 2004 and June, 2005 and this data was analyzed with statistical program, "SPSS® 11.0 for Windows®. Data was analyzed with chi-square tests to evaluate the significance between the originator and generic drug companies.

RESULTS

Number of pharmaceutical companies involved in the study is shown in Table1. All of the participants (%100) of foreign drug companies think that data exclusivity will be a beneficial change (Table 2). There is a statistically difference in opinions according to the usefulness of data exclusivity between local and foreign drug companies ($\chi^2 = 21.760$; $p<0.05$).

There are promoting views that data exclusivity will cause decrease in market share of generic companies. So it is expected that 60% of local companies (most of them are generic manufacturers) think data exclusivity will not be a beneficial change. However, 20% of local companies stated that data exclusivity would be a beneficial change. These companies were mostly the importers of original drugs. Furthermore, there were generic drug manufacturers thinking in the same way. These companies believe that data exclusivity will be an inducement for research and development activities in pharmaceutics. Most of the foreign companies that replied this question were the original manufacturers. Data exclusivity is being fiercely advocated by multinational research based pharmaceutical companies operating in developing countries such as Israel, Jordan, Turkey, India, and Thailand (9). So all of the foreign companies answered this question as "data exclusivity will be beneficial".

Table 1. Pharmaceutical companies that involved in the study – originator or generic; manufacturer or importer

	Number of Firms	%
Original drug manufacturer	15	46.9
Generic drug manufacturer	12	37.5
Both original and generic drug manufacturer	2	6.3
Original drug importer, generic drug manufacturer	2	6.3
Original drug importer only	1	3.1
Total	32	100

Table 2: General opinions of the pharmaceutical companies on data exclusivity

			General opinions of data exclusivity		
			beneficial	not beneficial	partially beneficial
	Local Company	Number/ %	3/ 20.0%	9/ 60.0%	3/ 20.0%
	Foreign Company	Number/ %	17/ 100.0%		
Total		Number/ %	20/ 62.5%	9/ 28.1%	3/ 9.4%

(Pearson chi-square=21.760; $p<0.05$)

Table 3. Opinions of the companies about the of data exclusivity

			Duration of		
			6 years	10 years	Less than 6 years
	Local Company	Number/ %	10/ 66.7%	3/ 20.0%	2/ 13.3%
	Foreign Company	Number/ %	12/ 70.6%	5/ 29.4%	
Total		Number/ %	22/ 68.8%	8/ 25.0%	2/ 6.3%

(Pearson chi-square=2.567; $p>0.05$)

There was no significant difference between the answers of local and foreign companies about the duration of data exclusivity. Both local and foreign companies predicted 6 years data exclusivity, because it is accepted period in most countries and the minimum period in EU legislation (χ^2 = 21.760; $p<0.05$) (10).

Table 4: Opinions of the companies whether data exclusivity is an incentive factor to invent an original drug by Turkish local companies or not

			Can data exclusivity be an incitement to invent an original drug		
			Yes	No	No idea
	Local Company	Number/ %	9/ 60.0%	5/ 33.3%	1/ 6.7%
	Foreign Company	Number/ %	10/ 58.8%	2/ 11.8%	5/ 29.4%
Total		Number/ %	19/ 59.4%	7/ 21.9%	6/ 18.8%

(Pearson chi-square=3.895; $p>0.05$)

There was no significant difference between the answers of local and foreign companies about whether data exclusivity is an incentive factor to invent an original drug by Turkish local companies or not (χ^2 = 3.895; $p>0.05$). Although Turkish local companiesare not able to invent original drugs for today (11). However, 60% of local companies that replied the questionnaire think that data exclusivity has an encouraging role on research and development. Protection of intellectual property rights in drug resulted in research and development activities of generic manufacturers to invest more. An Italian pharmaceutical company, Menarini Group, was only producing generic drugs in late 1970's. After the acceptance of patent protection in 1978, Menarini Group increased the sources for investment of research and development. Today, this company is the 9th largest pharmaceutical

company in the world and has its own original drug products (12). This success is a result of the investments in research and development by force of intellectual property rights protection for drugs.

Table 5. Opinions of the companies about the effects of data exclusivity on the future export potential of local companies

			Data exclusivity on the future export potential of local companies			
			Exportation increases	Exportation decreases	Exportation is not effected	No idea
	Local Company	Number/ %	9/ 60.0%	6/ 40%		
	Foreign Company	Number/ %	12/ 70.6%		4/ 23.5%	1/ 5.9%
Total		Number/ %	21/ 65.6%	6/ 18.8%	4/ 12.5%	1/ 3.1%

(Pearson chi-square=11.348; $p<0.05$)

There was a significant difference between the answers of local and foreign companies on this question ($\chi^2 = 11.348$, $p<0.05$). However, most of the firms (65.6%) replied this question positively as "data exclusivity can increase the exportation".

Table 6. Opinions of the companies about the continuity of equivalent drug policies

			Will the equivalent drug policies go on with data exclusivity?	
			Yes	No
	Local Company	Number/ %	5/ 33.3%	10/ 66.7%
	Foreign Company	Number/ %	16/ 94.1%	1/ 5.9%
Total		Number/ %	21/ 65.6%	11/ 34.4%

(Pearson chi-square=13.052; $p<0.05$)

There is a significant difference between the answers of local and foreign companies about the equivalent drug policies ($\chi^2 = 13.052$; $p<0.05$). Equivalent drug policies is known as "cheap drug" application, and according to this system, reimbursement organizations will only pay at most 30% more from the cheapest drug in the market. Naturally, original products are more expensive than generic products. It seems that cheap drug application reduced the earnings of foreign drug companies and caused the original manufacturers to worry. Some references stated that the most important reason of data exclusivity debate is the cheap drug application: "Data exclusivity debate has started with the radical changes on cheap drug applications of Bağ-Kur (one of the biggest governmental reimbursement organization) in 2002 (13)."

Table 7. Opinions of the companies about the estimated loss of governmental organizations in the first 6 year of data exclusivity period

			Estimated 6 year loss of governmental organizations		
			1 billion $	100 million $	No idea
	Local Company	Number/ %	6/ 40.0%	1/ 6.7%	8/ 53.3%
	Foreign Company	Number/ %			17/ 100.0%
Total		Number/ %	6/ 18.8%	1/ 3.1%	25/ 78.1%

(Pearson chi-square=10.155; $p<0.05$)

The amounts which are stated in the question (1 billion $ and 100 million $) were estimated by "The Association of Research Based Pharmaceutical Companies" and "Turkish Pharmaceutical Manufacturers' Association. There are significant differences in opinion between the answers of local and foreign companies about the estimated loss of data exclusivity to governmental organizations ($\chi^2 = 10.155$; $p<0.05$). Local companies think that the loss will be more. However 78.1% of all participant companies have "no idea" to this question. It shows that financial references about data exclusivity are not sufficient.

Table 8. Opinions of the companies about whether the public information on data exclusivity is sufficient or not

Public information on data exclusivity	All companies	%
Public information is sufficient and objective	1	3.1
Public information is not sufficient and there is need for more objective studies	30	93.8
No idea	1	3.1
Total	32	100

According to the results of this question, publications on data exclusivity issue in Turkey are not sufficient and more studies must be done on the subject. There are some inconsistencies and insufficiencies about the publications of data exclusivity. Definitions, effects and policy explanations about data exclusivity are uncertain and variable in Turkey. Some of the reasons of this uncertainty are;

- Insufficient statistical data in Turkey,
- Expensiveness of studying on data exclusivity,
- Insufficient number of intellectual property rights specialists,
- Variability and changes in legislation,
- Big financial dimensions that every organization can be related with it.

Table 9. Several opinions of the local and foreign companies about data exclusivity in Turkey

		1.	2.	3.	4.	5.	6.	7.
Local company	Number/	6/	37	9/	6/	12/	2/	2/
	%	40	20	60	40	80	13.3	13.3
Foreign company	Number/	-	-	5/	12/	8/	14/	-
	%	-	-	29.4	70.6	47.1	82.4	-
χ^2		23.93						
p		<0.001						

1. Local companies will be affected from data exclusivity too much and may be up against bankruptcy.
2. Local raw drug material manufacturers may be up against bankruptcy.
3. Local companies survive but their situation will be worse.
4. Local companies may increase their market share with research and development activities.
5. Local and foreign companies will get cooperated.
6. Foreign capital to wards to Turkey will be increased.
7. Expected capital income will not become true

By analyzing "Table 8", we can see there is significant difference in opinion between local and foreign companies about two subjects; surviving of local drug companies and foreign capital income (χ^2 = 23.93; p<0.001). Research and development studies in local drug industry, increased foreign capital income, easy market procedures on new original drugs and harmonization of European Union and Turkish Pharmaceutical Legislations are good sides of data exclusivity. But, as WHO says, intellectual property rights that are being applied with TRIPS agreement may have negative effects on public health (14).

DISCUSSION

This study shows that the original manufacturers think the data exclusivity is a beneficial change (100%) and will increase the exportation (70,6%); local companies will increase their market share with research and development (70,6%); foreign capital towards to Turkey will be increased (82,4%) and there will be no change in governmental procedures such as equivalent drug policies (94,1%). Basic research is not being done on health sciences in Turkey. Researchers can only find resources for formulation development and adaptation studies. It is impossible to invent an original drug by Turkish local companies today (11). Average cost of developing a new chemical is 880 million USD and this process takes 15 years (15). Encouraging the original drug manufacturers to invent safer and more effective molecules is important. Also Turkish generic drug companies aware of the importance of research and development activities with the collaboration of the universities.

Beneficial parts of data exclusivity in Turkey can be orientation of generic manufacturers to research and development activities, increasing foreign investments and accordance to the international agreements.

Data exclusivity application will have an impact on the future evolution of the industry. The long-term benefits could outweigh the costs of any shorter-term disruptions, and it should be recognized that this is not a "zero sum game" with original manufacturers winning and generic manufacturers losing. The beneficial effects of data exclusivity could create a stronger industry in favor of many stakeholders and of Turkey overall (16).

On the other side; TRIPS Agreement's requirements (like data exclusivity) may affect public health in a negative way (17). Most of the local companies involved in this study (60%) think that data exclusivity will not be a beneficial change and (40%) governmental organizations' estimated 6 year loss is about 1 billion USD. Access to essential drugs is part of the human right to health. Protecting

the original manufacturers and investing in research and development facilities are beneficial. But poorer populations in developing countries should not be expected to pay the same price for newer essential drugs as the wealthies do. (17).

CONCLUSION

Turkish Ministry of Health has accepted a data exclusivity model and the arguments is ended in Turkey for a while. According to this model, data exclusivity is not retrospective and it is limited with patent duration. Furthermore, original drug manufacturers explained that they wouldn't agree with a decision that is not retrospective.

Although data exclusivity may cause negative effects including the decrease in the market size of local pharmaceutical companies, in majority of local and foreign companies both perceive the data exclusivity as a necessary and beneficial change. Since the replies of questionnaire state that data exclusivity has positive effects in the long term such as increasing on investments of foreign pharmaceutical companies in Turkey, encouraging the local companies for more research and development activities.

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