The production of generic drugs after the expiry of patents: which reality in Algeria?

انتاج الأدوية الجنيسة بعد سقوط براءات الاختراع :أي واقع في الجزائر؟

Zoulikha Snoussi

[1]Laboratory of Industry, Corporate Organizational Evolution and Innovation, Djillali Bounaâma University, Khemis Miliana(Algeria), z.snoussi@univ.dbkm.dz

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Abstract:

This article studies the impact of the expiry of patents on the production of generic drugs in Algeria. For each molecule selected, we identified the number of locally made generic versions (NGFL), the age of the molecule (Mkt Age) and the number of years since the patent expires (Yrs Off). Then, our contribution takes place in the form of an econometric modeling from panel data for the period 2006 to 2011.

We found that (Mkt Age) and (Yrs Off) have no impact on (NGFL). Thus, we conclude that the algerien pharmaceutical industry does not take advantage of expired patents to develop its local production of generic drugs.

Key Words : patent ; generic drugs ; local production ; Algeria.

JEL Classification Codes: I18, L65, P14.

ملخص:

يهدف هذا المقال لدراسة أثر سقوط براءات الاختراع على انتاج الأدوية الجنيسة في الجزائر. بالنسبة لكل جزيء تم اختياره، حددنا عدد الأدوية الجنيسة المصنعة محليا (NGFL)، العمر التجاري للجزيء (Mkt Age) و عدد السنوات منذ سقوط براءة الاختراع (Yrs Off). بعدها قمنا بنمذجة اقتصادية في شكل نموذج "بانل" للفترة الممتدة من 2006 الى 2011.

· ***Corresponding author**: Zoulikha Snoussi, **e-mail:** snoussi25@yahoo.fr*

توصلنا الى أن (Mkt Age) و (Yrs Off) لا تأثير لهما على (NGFL) و عليه نستنتج أن صناعة الأدوية في الجزائر لا تستفيد من براءات الاختراع التي انتهت صلاحيتها لتطوير انتاجها المحلي من الادوية الجنيسة.

الكلمات الرئيسية :براءة الاختراع؛ الادوية الجنيسة؛ الإنتاج المحلي؛ الجزائر.

تصنيفات JEL: P14, L65, I18

1. INTRODUCTION

The drug, like any invention, is protected by a patent. Therefore, pharmaceutic laboratories that produce new drugs have exclusive rights to produce and market their product. Once the drug patent's expires (usually after 20 years), it becomes public property. When the patent expires and market exclusivity is lost, the drug's constituent molecule may be produced and sold by other companies, particularly in the form of generics. Thus, the production of generic drugs can only be developed after their patents expire.

Theoretically, it is accepted that patents on drugs are directly linked to the research and development activity, very costly, that only multinational pharmaceutical companies, also known as "big pharma" of developed countries, have the means to innovate. Other less developed countries could wait until patents expire before starting production of generic copies. In fact, in order to respond to an ever-increasing demand, Algeria remained, for years, highly dependent on the outside world. The growth of the drug market was mainly driven by imports. Indeed, between 2000 and 2011, the import invoice increased almost sixfold, from some US$ 400 million to more than US$ 2.8 billion. (Snoussi, 2013, p181). But the strategy of encouraging national production, which began in the 1970s, has just borne fruit because, in 2017, 73% of the national market in volume terms is covered by national production, compared to only 27% by imports. However, in terms of value, the national market remains dominated by

imports, which account for 52% of the total market. (Conseil de la concurrence, 2019, p48)

In addition, despite the increase in national production[1], the molecules produced are still mostly generics; between 2011 and 2015, the share of generics in national production was between 83% and 86%. This rate recorded a slight decrease in 2016 of 81.48% (Conseil de la concurrence, 2019, p48). The promotion of generics takes the form of a range of provisions; the pharmacist's right of substitution; financial incentives granted to private doctors and pharmacists to successively prescribe and dispense generics, the introduction of the Reference Rate system, faster registration procedures for generics, a ban on the import of locally manufactured drugs, etc.

Thus, if the national production of generics has known a significant expansion in last years, the aim of our paper is to know whether Algeria really takes advantage from patents that have fallen into the public domain to develop this production.

Our work consisted in a search in order to identify the molecules marketed in Algeria that have lost their patents internationaly. We selected 18 molecules registered in Algeria. For this selection, we referred to the database of the MHPHR (Ministry of Health, Population and Hospital Reform) listing all drugs registered in Algeria until December 31, 2010. For each molecule, we noted the number of locally manufactured generic versions (NGFL), the age of the molecule (Mkt Age) and the number of years since patent expires (Yrs Off). We conduct our study on a sample of 18 molecules and over a period from 2006 to 2011.

The data collection has enabled us to propose an econometric model based on panel data in order to estimate the impact of patent expiry on the local manufacturing of generic drugs. So to do, we relied on the literature initiated by the pioneering work of (Frank & Salkever, 1992) which we detail below.

The article is organized as follows. In the first section, we provide a review of the theoretical and empirical literature relative to the impact of

[1] From 28% in 2012 and 19% in 2013, growth in national drug production recorded 43% in 2016.

patent expiry on drug prices on the one hand, and on other variables on the other. The second section is dedicated to the study of the impact of patent expiry on the local production of generic drugs in Algeria. In the third section, we discuss the results found. Finally, in a last section, we conclude and propose some recommendations for public drug policies.

2. Literature review

In this section, we provide a brief review of the theoretical and empirical literature of the main works dealing with the impact of expiry of patent on different variables.

The study of the impact of expiry of patent, or indirectly of the entry of generics, has led to a large amount of research in several directions. The main one concerns the impact of generic entry on drug prices by distinguishing, in most studies, between originator (brand name drugs) and their corresponding generics. Other routes have also been taken to measure the impact of expiry of patent on other variables such as demand, markets share or the behaviour of pharmaceutical companies.

2.1 Impact on drug prices

To explain the positive correlation between generic entry and the price level of the originator drugs, (Frank & Salkever, 1992) propose an explanation in terms of market segmentation based on the persistence of originator prescribing by doctors. They assume that there are two types of consumers on the market: the first type of consumers is insensitive to the price of generics and consider the quality of the originator drug better than generics. The others are sensitive to the prices of both drugs, and therefore less sensitive to the perceived quality. Generic entry therefore implies a decrease in demand for the originator, all other things being equal. In order to maximise its profit, the originator company increases its price.

In the same ideas order, another explanation is given by (Kong, 2008) to the "paradox of generic competition". He assumes that consumers in the drug market are segmented into consumers with the best coverage who are considered insensitive to the price, and those less covered who are more sensitive to the price. Consumers of the first type

don't care much about drug costs since they are covered by health insurance. Therefore, their doctors may prescribe them the original drug or its generic version. However, price-sensitive consumers will opt for generic drugs because they are cheaper.

(Caves, Whinston, Hurwitz, Pakes, & Temin, 1991) provide a descriptive analysis of the effects of patent expiry and generic entry. Using seven therapeutic classes encompassing thirty drugs that lost their patents between 1976 and 1987 in the US, the authors compare the change in prices of originator drugs before and after generic entry. They find a relatively small negative relationship on average (4.5%).

(Grabowski & Vernon, 1992) study the effect of generic entry on the prices of 18 drugs that lost their patents between 1983 and 1987. Empirical results indicate that two years after the entry of the first generic, the price of the originator drug increases by 11%.

In a sample of 32 drugs that were off-patent between the 1980s and 1985, (Frank & Salkever, 1997) show that each new generic entry is associated with a slight increase of 0.7% in the price of originator drugs, while each new generic entry reduces the average price of the generic drug of 5.6% to 7.2%.

(Aronsson, Bergman, & Rudholm, 2001) studied twelve originator medicines that face generic competition in the Swedish market. They find that the number of generic competitors has a positive and significant impact on the originator-to-generic price ratio (PP/PG), which means that the average price of generic drugs decreases and the PP/PG increases.

Focusing on the transaction level of anti-infectives in retail pharmacies for the period 1984-1990, (Wiggins & Maness, 2004) show that prices of medicines (without distinguishing between originator and generic types) decrease with the increase in the number of sellers. Thus, prices fall by about 83% when the number of vendors increases from 1 to between 6 and 15 vendors. This decrease is followed by another 52% when the number of vendors increases from 6 to 15 to more than 40.

Based on the theoretical model of (Frank & Salkever, 1997), (Regan, 2008) conducted an empirical test of market segmentation theory. She

proposes a test of the relationship between patent expiry and prescription drug prices. She finds that each generic entry into the market causes on average 1% increase in the price of the originator. Furthermore, she clarifies that price competition in the prescription drug market is limited to the generic market.

Also for the United States, using a simultaneous equation model, (Saha, Grabowski, Birnbaum, Greenberg, & Bizan, 2006) analysed a sample of panel data of 40 originator drugs that known generic competition for the first time between July 1992 and January 1998. They find that each additional generic entry is associated with an average decline of 0.2% in the originator prices.

On the Tunisian drug market, using data for four molecules for the period from the third quarter of 2002 to the fourth quarter of 2008, (Ayadi, 2009) shows that the number of generics affects negatively the price of the originator drug: each additional generic leads to a reduction of approximately 9.8% in the price of the deflated originator drug. This reduction is less significant (4.1%) for the average price of generics.

Based on econometric modelling using panel data for the period 2006-2011, (Snoussi, 2013) has shown that the increase in the number of generic competitors on the Algerian market leads only to a small decrease in generic prices of 1.4%. However, the impact is neutral on originator prices.

2.2 Impact on other variables

(Conti, Rosenthal, Polite, Bach, & Tina Shih, 2012) examined the effect of generic entry on the choice of chemotherapy for the treatment of metastatic colorectal cancer (CMCC) between 2006 and 2009 using autoregressive moving average modelling. A representative sample of oncologists and cancer patients (age $\geq$ 65 years) was used to estimate the magnitude and significance of the impact of the generic entry of "irinotecan", in February 2008, on the number of administrations of "irinotecan" versus "oxaliplatin" (its originator). The authors found that the use of generic "irinotecan" resulted a decrease of 17% to 19% in use in elderly patients with CMCC compared to "oxaliplatin".

Based on ambulatory antibiotics data prescribed by the German health insurance scheme and on data from a German university hospital for use of antibiotics in hospitals, (Kaier, 2012) investigated whether the demand for specific antimicrobial agents is driven by prices that fall as generics become available after patent expiry. A time-series approach was therefore used to explore the price elasticities of demand for two different classes of broad-spectrum antimicrobials (fluoroquinolones and cephalosporins). The authors find that patent expiry is generally followed by a significant decrease in the price of antibiotics. In the ambulatory care sector, all the antibiotics studied had significant negative elasticities of demand compared to their own prices. However, in hospitals, only a few antibiotics showed significant price elasticities, although the price decreases were greater than in the other sector.

(Suh, Manning, Schondelmeyer, & Hadsall, 2006) were interested in analyzing the effect of multi-source drug[2] entry on post-patent expiry price competition in the pharmaceutical industry. The originators[3] and their multiple source drugs were selected from among 35 chemical entities whose patents expired between 1984 and 1987. The authors' findings suggest that, after patent expiry, prices of "originator" drugs continue to increase, while prices of multiple source drugs decrease. However, four years later, sales of "originator" drugs declined by 12% in dollar terms and 30% in volume terms, while sales of multiple source drugs doubled in dollar terms and tripled in volume terms. They represented for about one-quarter (in dollars) and half (in quantity) of the total market three years after their entry. They conclude that after patent expiry, competition between multiple source drugs is tough in the price-sensitive sector, but indirect with the originator in the non-price-sensitive sector. They explained that

[2] The multi-source drug is a drug available from one brand name manufacturer and several generic manufacturers.

[3] When a patent for a brand name drug expires, the US Food and Drug Administration (FDA) offers a period of exclusivity (usually six months) to one company (the same company that produced the brand name drug or another company) to manufacture the generic drug, there is a single source or "originator". These drugs cost more than other generics because they are manufactured by a single pharmaceutical company for a set period of time.

"originators" have first-mover advantages and are therefore in a less price-sensitive market after generic entry. On the contrary, multi-source drugs target the price-sensitive sector and benefit from their lower price advantages.

(Ching, 2000) wanted to explain the evolution of pharmaceutical markets after patent expiry. Using a dataset detailing the evolution of prices and market shares of 31 chemical entities between 1984 and 1990, the author estimated the distribution of consumer preferences that determine how consumers assess prices when choosing between originator and generic drugs. Based on his estimates using data from two markets, flurazepam and temazepam, the author considers that learning plays an important role in explaining the slow evolution of generic market share. He adds that consumer heterogeneity explains, to a large proportion, the pricing model in which originator prices increase in response to generic entry.

3. Econometric modeling

Our empirical work is structured around three points. First, we present the approach adopted for the collection of data on the Algerian drug market. Then, we present the equations to be estimated in order to assess the impact of patent expiry on the number of locally manufactured generics. Finally, we present the results of the estimation of this equation for the Algerian case and propose economic interpretations as well as suggestions and recommendations regarding the Algerian drug policy.

Our work consisted in a research in order to identify the molecules marketed in Algeria that have lost their patents internationally. We selected 18 molecules registered in Algeria. For this selection, we referred to the database of the MHPHR listing all drugs registered in Algeria as of December 31, 2010. For each molecule, we noted the number of locally manufactured generic versions (NGFL), the age of the molecule (Mkt Age) and the number of years since patent expiry (Yrs Off). We conduct our study on a sample of 18 molecules and over a period from 2006 to 2011.

The data collection allowed us in a second step to propose an econometric modeling on panel data in order to estimate the impact of

patent expiry on the local manufacturing generic drugs. So to do, we referred to the literature initiated by the pioneering work of (Frank & Salkever, 1997) which we detail below.

It is recognized that the number of generic entrants depends on the age of the molecule on the market (Mkt Age), the number of years since patent expiry (Yrs Off) and the size of the market, as measured by sales volumes before patent expiry. Thus, Frank and Salkever use three estimation models. In the first model, the number of generic entrants (NMFT) is assumed to be exogenous. In the other two models, NMFT is endogenous under the assumption that NMFT varies over time. The third model incorporates the size of the market as a variable (Qpre), the age of the market (Mkt Age) and the number of years since patent expiry (Yrs Off). They consider that the time elapsed since patent expiry has an indirect effect on the price of the originator drug through the number of generics on the market. In our analysis, in the absence of data, we consider just the first two variables: (Mkt Age) and (Yrs Off). Thus, our model is written as follows :

$$NGFL_{it} = \alpha_0 + \alpha_1 \text{ Mkt Age}_{it} + \alpha_2 \text{ Yrs Off}_{it} + \alpha_3 T + \varepsilon_{it}$$

In this section, we estimate the equation that measures the impact of the age of the molecule (time since first commercialization) and the time since patent expiry of the molecule on the number of generic versions manufactured locally. Table 1 provides descriptive statistics for the different variables used.

Table 1. Summary of descriptive statistics

	Observa —tions	**Mean**	**Standard deviation**	**Mini- -mum**	**Maxi- -mum**
NGFL	108	2,69	3,31	0	15
MktAge	108	18,48	6,90	8	35
YrsOff	108	6,98	6,6	0	21

Source: Results provided by Stata12.

The number of observations for the different variables is the same: it is therefore a cylindrical panel. There is a high degree of heterogeneity during the period analysed. The number of locally produced generics (NGFL) varies between 0 and 15. MktAge varies between 8 and 35, which means that the molecules studied range from the oldest to those recently marketed on the drug market. As for the YrsOff variable, it ranges from 0 to

21, which explains that in our sample, there are molecules that have fallen into the public domain in the past and others that have just lost their patents during the observation period (between 2006 and 2011) (Table 1).

3.1 Test for the presence of individual effects

The first step is to test for the presence of individual effects in our data and thus test the hypothesis of heterogeneity in our model between the originator drugs and confirm or deny the use of the OLS method. The null hypothesis of this test is that there are no individual effects. The results of the Fisher test on our model are as follows: F (17.87) = 68.90 with Prob > F = .0000. Fisher's statistics reject in our model the H0 hypothesis. It then appears that there are indeed drug-specific effects. Therefore, the use of the OLS method will be biased and we must choose one of the two models "Fixed Effects" or "Composite Errors", after the Hausman test result, for the treatment of panel data (Table 2).

In what follows, we propose a battery of standard tests to determine the best model to use in our estimates of the number of locally produced generics equation.

3.2 Hausman test

The Hausman test refutes the hypothesis that there is no correlation between the random term and the explanatory variables of the model (P-value= 82.63% >5%). The results of the Hausman test allow us to opt for the compound error model (CE) because Prob>chi2 = 0.8263.

However, before validating the model, it should be determined whether it adequately verifies the Gauss-Markov hypotheses. Therefore, we check the homoscedasticity as well as the absence of autocorrelation between the residuals.

3.3 Breush-Pagan Heteroskedasticity Test

We use the Breusch-Pagan test, which consists of retrieving the residuals of the regression we wish to test, generating the squares of the residuals, and finally performing a regression of the squares of the residuals on our independent variables to test whether the coefficients are jointly significant. The null hypothesis of these tests stipulates the absence of heteroskedasticity. The result of the Breush-Pagan test accepts the

hypothesis of absence of heteroskedasticity at the 5% threshold (Chi2(1)=0.02) with p> 0.8876). We are then in the presence of a homoscedastic model.

3.4 Intra-individual auto-correlation test (auto-correlation of errors)

The Wooldridge auto-correlation test checks whether the errors are auto-correlated in an autoregressive form of order 1, AR(1). The null hypothesis is the absence of error autocorrelation. The results founded F(1,17)= 35,773 with (p>0.0000) suggest acceptance of the alternative hypothesis, which allows us to conclude that auto-correlation is present.

Since we performed all the tests for heteroscedasticity and auto-correlation and found that our model has no heteroscedasticity but an auto-correlation between residuals of first order is detected. Therefore, we estimate our model with the necessary autocorrelation corrections represented in Stata by the command "xtregar". So to do, we first perform the Spearman correlation test between the explanatory variables. The results of this test, presented in Table 3, show a strong correlation between the two explanatory variables MktAge and YrsOff. Thus, we estimate our model twice, once without the first variable and once without the second explanatory variable (Table 4).

We find that among the variables, only the Time variable is statistically significant at the 5% threshold and of expected sign. Thus, the age of the molecule (MktAge) and the time since patent expiry (YrsOff) have no impact on the number of locally produced generics (NGFL). In addition, local production of generics increases over time.

Table 2. Regression of locally manufactured generics

	OLS	Fixed effects	Error Compounds
MktAge	0,277 (0,011)	-0,00007 (1,000)	**0,049** **(0,628)**
YrsOff	-0,279 (0,013)	-0,055 (0,717)	**-0,062** **(0,580)**
T	0,369 (0,048)	0,444 (0,016)	**0,403** **(0,000)**
R2 **Within** **Between** **Overall**	0,1025	0,3983 0,0014 0,0399	**0,3973** **0,0580** **0,0646**
F	3,96 (0,0102)	19,19 (0,0000)	
Hausman			**Chi2(3)= 0,9** **Prob> chi2=0,8263**

Source: Done by the author based on the results provided by Stata 12.

Table 3. Spearman matrix between explanatory variables

	MktAge	YrsOff	T
MktAge	1,000		
YrsOff	0,8762	1,000	
T	0,2623	0,2642	1,000

Source: Results provided by Stata 12

Table 4. Summary of the model

	EC corrected	EC corrected
MktAge	0,036 (0,626)	/
YrsOff	/	-0,029 (0,766)
T	0,35 (0,000)	0,41 (0,000)

Source: Done by the author based on the results provided by Stata 12.

In the first column, the estimation was done without taking into account the variable YrsOff. In the second column, the estimation is made without taking into account the variable MktAge.

4. Economic Interpretation

Using the results found in Table 5, we say that the age of the molecule and the time since patent expiry have no impact on the number of locally

produced generics. However, the impact of the time recorded is positive; with each passing year, the number of generics manufactured by national companies increases by 35% to 40%. Therefore, we understand that the local pharmaceutical industry does not take advantage of expired patents or old molecules to produce more generics which, in fact, depend in their evolution on time alone.

Table 5. Summary of the results of estimating the impact of patent expiry on national production

		NGFL
Impact of expiry of patent	**MktAge**	No impact
	YrsOff	No impact
	Time	Increase by 35% to 40%

Source: Done by the author based on the results provided by Stata 12.

From the results obtained in this study, we can conclude the following points. First, it seems that Algerian pharmaceutical companies do not use patent information.[4] This is justified, on the one hand, by the lack of national structures or even the absence of specialized research services that ensure and facilitate the dissemination and access of companies to information, and on the other hand, by the indifference of national companies to seek useful information due to a lack of financial, human and technical means or simply due to the absence of a watch culture[5] in our companies. Secondly, our conclusion can be justified by the incompetence of the manipulation of the techniques and the manufacturing processes of the molecules due to the lack of use and mastery of the know-how and new technologies. Finally, rigid regulations, which make the registration procedures for generics long and costly, may be a good cause to discourage

[4] Patent information is a term referring to the commercial, legal and technical information disclosed in the patent application as well as in the course of examination and the issuance of the patent.

[5] It is the act of monitoring the business environment in order to identify and collect information useful for preparing the future, detecting threats and seizing development opportunities. It is used to analyse the state of a market, emerging technologies, the positioning of the competition and the evolution of legislation.

local industrialists to finding out about expired patents in order to start producing generics.

5. CONCLUSION AND RECOMMENDATIONS

The aim of this article is to find out whether the Algerian pharmaceutical industry is taking advantage of expired patents to develop its local production of generic drugs. Thus, we have estimated the effect of patent expiration on the production of generics in Algeria. We find that the number of generics produced in Algeria increases by 35% to 40% over time, but not with the age of the molecule, nor with the time elapsed since the expiration of the patents. Thus, we conclude that the expiration of patents has no impact on the local production of generics.

Based on the above insights and in order to allow an increase in local production of generics while taking advantage of expired patents, we propose some recommendations.

First of all, the aim is to improve access to patent information, which involves several tasks, among others:

- Dissemination of patent information which can be done in several ways; either through data exchange agreements between the Algerian National Institute of Intellectual Property and other intellectual property offices (national, regional or international) [6], or through the sale of patent data to the private sector or through online databases ;
- Training and awareness-raising strengthening to make Algerian pharmaceutical companies more aware of the importance of using patent information for business competitiveness. Among the recommended solutions, the organization of open days, study days and seminars addressing the issue of useful information in the knowledge economy, as well as patent information retrieval techniques and, more generally, the issue of pharmaceutical patents and access to drugs ;

[6] These include: EPO (European Patent Office), UPSTO (United States Patent and Trademark Office), WIPO (World Intellectual Property Organization), etc.

- The development of tools to facilitate patent searches; CD-ROM databases are very practical for documentary searches. Also, online databases are useful. Access to such databases is not limited to national borders.

Secondly, partnerships and technology transfer in the private pharmaceutical industry should be encouraged. [7] This will enable local companies to benefit from new technologies and access international scientific and technical knowledge. There are a number of tools that can be used:

- The "Turnkey" formula where the seller of the technology undertakes to deliver a complete industrial package to the buyer within a prescribed period of time ;
- The "Product in Hand" formula designed to compensate for the inability of certain buyers to make the best use of the information received. For this category of contract, the seller undertakes not only to deliver, install and start up a functioning installation, but also to guarantee production capacity and quality for a certain period of time, and generally with local personnel that the seller must train for this purpose. This type of contract therefore implies prolonged technical assistance ;
- The "Market in hand" contract in which the seller underkates not only to provide a "turnkey" installation, but also to purchase part of its production for a period of time ;
- Joint venture in which a small number of partners join together by sharing the capital of the company. In addition, a joint venture involves a technical, managerial, financial and legal association ;
- Foreign Direct Investment (FDI) resulting in the creation of a company abroad or the acquisition of a stake in foreign firms. Thus, FDI remains the most effective means of technology transfer between industrialized countries and developing countries.

[7] For the public pharmaceutical sector, the only operator Saidal is advanced in the conclusion of various technology transfer contracts, including Joint Ventures, pharmaceutical manufacturing agreements and licensing agreements.

Finally, action will have to be focused on facilitating and making more flexible the registration and marketing procedures for locally manufactured generic products by requiring less paper, reducing costs and shortening the time taken to process files. At the same time, more limited conditions on the registration of imported products will have to be put in place through strict administrative and regulatory procedures to discourage foreign laboratories from registering their drugs in Algeria. [8]

6. Bibliography List

- Aronsson, T., Bergman, M.-A., & Rudholm, N. (2001). The impact of generic competition on brand name market shares-Evidence from micro data. *Review of Industrial Organization, 19*(4), 425-435.
- Ayadi, I. (2009). Impact de la reforme d'assurance maladie en Tunisie sur l'offre et la demande des médicaments. *Thèse de Doctorat en Sciences Economiques*. Université de Sfax en cotutelle avec l'Université Paris Dauphine, France.
- Caves, R.-E., Whinston, M.-D., Hurwitz, M.-A., Pakes, A., & Temin, P. (1991). Patent expiration, entry, and competition in the US pharmaceutical industry. Brookings Papers on Economic Activity. *Microeconomics, 91*(1), 66-80.
- Ching, A. (2000). Dynamic equilibrium in the US prescription drug market after patent expiration. *Econometric Society World Congress.*
- Conseil de la concurrence. (2019). *Etude sectorielle sur la concurrentiabilité du marché des médicaments à usage humain en Algérie.* Algérie.
- Conti, R.-M., Rosenthal, M.-B., Polite, B.-N., Bach, P.-B., & Tina Shih, Y.-C. (2012). Infused chemotherapy use in the elderly after patent expiration. *Journal of Oncology Practice, 8*(3), 18-23.
- Frank, R.-G., & Salkever, D. (1992). Pricing, patent loss and the market for pharmaceuticals. *Southern Economic Journal, 59*(2), 165-179.
- Frank, R.-G., & Salkever, D. (1997). Generic entry and the pricing of pharmaceuticals. *Journal of Economics and Management strategy, 6*(1), 75-90.

[8] Several obstacles are placed by different countries to prevent national laboratories, both private and public, from registering drugs in their countries. Egypt, Tunisia and Jordan include the requirement that the drug being registered must not be manufactured locally in these countries, and the registration file must be accompanied by the bioequivalence file, which is considered to be a very complex and costly, as only one file costs $120,000. In Saudi Arabia and the Gulf countries, the rules applied for drugs registration are the same as those applied by the American food and agricultural circle on medical products, whether local or imported.

- Grabowski, H., & Vernon, J. (1992). Brand loyalty, entry, and price competition in pharmaceuticals after the 1984 drug act. *Journal of Law & Economics*(35), 331-350.
- Kaier, K. (2012). The impact of pricing and patent expiration on demand for pharmaceuticals: an examination of the use of broad-spectrum antimicrobials. *Health Economics, Policy and Law, 8*(1), 7-20.
- Kong, Y. (2008). Competition between Brand-name and generics: analysis on pricing of brand-name pharmaceutical. *Health Economics, 85*(1), 591-606.
- Regan, T. (2008). Generic entry, price competition and market segmentation in the prescription drug market. *International Journal of Industrial Organisation*(26), 930-948.
- Saha, A., Grabowski, H., Birnbaum, H., Greenberg, P., & Bizan, O. (2006). Generic Competition in the U.S. Pharmaceutical Industry. *International Journal of the Economics of Business, 13*(1), 15-38.
- Snoussi, Z. (2013). L'accès aux médicaments en Algérie : une ambiguïté entre les brevets des multinationales et le marché des génériques. *These de Doctorat en Sciences Economiques*. Chlef, Algerie: Universite Hassiba Benbouali.
- Suh, D.-C., Manning, W.-G., Schondelmeyer, S., & Hadsall, R.-S. (2006). Effect of multiple-source entry on price competition after patent expiration in the pharmaceutical industry. *Health services research, 35*(2), 529-547.
- Wiggins, S.-N., & Maness, R. (2004). Price competition in pharmaceuticals: the case of antiinfectives. *Economic Inquiry, 2*(2), 247-263.