The Search for New Drugs: A Theory of RD in the Pharmaceutical Industry

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A Theory of R&D in the Pharmaceutical Industry

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The paper formalizes, in a rigorous manner, the concept of information externalities, by modeling R&D activities as the process of searching for a drug to treat a disease, with R&D activities being modeled from the perspective of the theory of optimal search. In conventional models of patent design, only one brand - the brand with the highest quality - is available on the market at any time. Furthermore, demand is completely inelastic: each consumer, regardless of income and regardless of the price of the brand offered on the market, buys exactly one unit of the brand. In this model, which is a dynamic model in continuous time, several differentiated products - the products whose patents are still in force and the products whose patents have expired - are available at any time on the market. Furthermore, the demand for a brand depends on income, its own price, and the prices of the other brands. The analyses of R&D as well as the impact of the cost and the quality of newly discovered drugs on the market are represented under this framework, when the pharmaceutical firms with an active drug discovery program behave strategically in both R&D and in the product market.

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1 Introduction

In the economics of science and technology, economists distinguish between basic research and applied research. The objective of basic research is to increase our knowledge about natural phenomena, not to develop specific applications of this stock of knowledge for pecuniary gains. However, applied research – often called R&D or innovation in the economic literature – is driven by profits, and a firm carries out applied research in order to develop a new product or to find a more efficient production process. Another difference between basic research and applied research is that the discoveries of basic research are widely published and freely available to all researchers, while the results of R&D activities are jealously guarded secrets of the organizations that discover them in their efforts to appropriate all the benefits from these discoveries.

The economic analysis of basic research concentrates on the social value of the increase in the stock of fundamental knowledge. The social value of an increase in the stock of fundamental knowledge is difficult to measure, or even to predict. Because basic research takes place at the frontier of knowledge, the economic benefits of a program of basic research are highly uncertain. Furthermore, because scientific discoveries are difficult to establish or to defend, it is almost impossible to define the property rights of these discoveries. The difficulty involved in the definition of property rights in basic research implies that discoverers of new fundamental knowledge cannot appropriate all the commercial benefits of their research, and this form of market failure is the basis for the assertion that the level of investment in basic research is socially sub-optimal. This fact is reflected in the modest share of basic research in the R&D budget of profit-driven firms. Yet for a program of basic research, the social value can greatly exceed its private value because advancements in fundamental knowledge constitute important inputs in many applied research programs and innovations.

Although R&D is profit-driven and mission-oriented, it shares one important characteristic with basic research: information externalities. The information generated by the R&D activities of a firm might help other firms in their search for a new product or a new process with lower costs. Revealing the results of its R&D activities to rival firms reduces a firm's competitive edge in its competition for profits and market share. This is the reason why firms keep the results of their R&D activities secret. However, rival firms can appropriate the fruits of the R&D activities of

other firms through imitation, reverse engineering, or information spillovers. These factors tend to reduce the incentive of a firm to carry out R&D activities, and a solution to this problem is to offer some protection to a firm's innovation by granting it a patent.

Nordhaus (1969) was the first researcher to offer a rigorous analysis of the fundamental trade-off between static efficiency and dynamic efficiency in the design of patent policy. A patent gives its owner the intellectual property right to exploit the fruit of her discoveries, which encourages innovation, and thus benefits society. This is the source of dynamic efficiency behind the granting of a patent. However, offering protection to an innovation allows the holder of the patent to exercise monopoly power, which is the source of static inefficiency. The model of Nordhaus, op cit., deals with the length of a patent, i.e., the number of years that the patent is in force.[2] It proposes complete protection of an innovation for a limited number of years, and can be taken as a simple description of the patent system in its original purpose. However, since the pioneering work of Mansfield (1961), researchers have found an overwhelming volume of evidence on the inability of patents to prevent imitation. According to Mansfield (1984), about 60% of patented products were successfully imitated within four years of patenting. Nordhaus (1972) dealt with the issue of imitation by adding a second dimension – *patent breadth or patent width* – to his original model. Intuitively, the patent breadth captures the minimum degree of novelty relative to the product purportedly protected by the patent that a rival product must possess so that it can be judged as not infringing on the patent.

Although the concept of patent breadth is intuitively appealing, its meaning is vague. Nordhaus (1972) deals with process innovation, and the breadth of a patent is taken as the fraction of cost reduction not freely flowing to rival firms through spillovers. Klemperer (1990) analyzed patent breadth in the context of a model of spatially differentiated products. The distance in space between the patent holder's product and a rival product represents the transport cost that a consumer must pay if she buys the rival brand. The breadth of a patent is defined as the radius beyond which a rival product is considered as not to infringe upon the patent. Klemperer took the prize of the patent, i.e., the discounted profits enjoyed by the patent holder, as given, and determined the length and breadth of the patent that minimizes the social cost subject to the

[2] In the US, the statutory life of a patent is about 17 years.

constraint that the patent holder earns the given prize. In the model of Gilbert and Shapiro (1990), patent breadth is simply defined as the flow rate of profit that a patent holder is allowed to earn while the patent is in force. The model is in reduced form, and the optimal length and breadth for the patent are found by maximizing discounted social welfare subject to the constraint that the patent holder is allowed to earn a certain level of profits. What this level of profits is was not specified by these researchers; neither was it explained in Klemperer's model. The varied definitions of patent breadth in the literature lead to an array of bewildering results. In some cases, the optimal patent has maximum length, but minimum breadth. In other cases, it is the opposite result. And in some other circumstances, the length-breadth mix makes no difference.[3] A consensus on the definition of patent breadth is yet to emerge.

In the earlier literature on patent design, all efforts were concentrated on finding the optimal length and breadth of a patent. The role of information externalities was not considered. Indeed, one of the conditions for granting a patent is that the holder of the patent must provide a disclosure of all the technical information that enables another researcher to replicate all the results claimed by the patent. Furthermore, the analysis was carried out in the context of a single innovation, and the inherent uncertainties in R&D activities were ignored. An exception was Scotchmer and Green (1990), who formulated a simple dynamic economic model that incorporates patent breadth and the incentive of firms to keep secret their R&D results.

In the model of Scotchmer and Green, there are only two possible innovations: a weak innovation and a strong innovation. The weak innovation represents a slight improvement in the quality of the product in question, while the strong innovation represents a more pronounced improvement of the product. The weak innovation yields one extra unit of welfare in perpetuity, while the strong innovation yields two extra units of social welfare in perpetuity. R&D activities are driven by research expenditures, and the discovery time is modelled as the arrival of a Poisson process. In the model, the information externalities were modelled in the following manner. The weak innovation requires one Poisson hit, while the strong innovation requires two Poisson hits. If a firm has obtained a Poisson hit, then it only needs another Poisson hit to obtain strong innovation. If the technical information obtained by the firm that obtained the first

[3] See Tandon (1982) for a discussion and a reconciliation of these contradictory results in a very simple model of the optimal length and breadth of a patent.

Poisson hit is disclosed to the other firm, which has not made any Poisson hit, then the latter firm can benefit from the information disclosure and only needs one Poisson hit to obtain strong innovation. On the other hand, if the former firm does not patent its weak innovation, then the latter firm must make two Poisson hits to obtain strong innovation.

O'Donoghue et al. (1998) formulated a model in which firms sequentially improve the products of each other through time, and technological progress occurs when a non-infringing innovation displaces a patented product. In this model, innovations are ideas that arrive in a random manner according to a Poisson process, and there is an infinite sequence of possible innovations. An idea is an ordered pair of numbers, with the first component representing the quality improvement of the innovation, and the second component the investment required to realize the innovation. If the investment embodied in the idea is not made, the idea is lost. There are no strategic interactions among firms, and a patent ceases to exist either when it reaches the end of its statutory life or when it is displaced by a better and non-infringing product.

The purported goal of a patent policy is to encourage technological progress. Yet, its impact on the pace of technological progress has largely been ignored by researchers in this field. Compared to the models of R&D in the literature on trade and technological progress, the model of R&D found in the literature of optimal patent design is much less sophisticated. In the research program on trade and technological progress of Eaton and Kortum (2001), ideas (discoveries) arrive in time according to a Poisson process whose parameter depends on the stock of knowledge – taken to be the cumulative effort of research workers. An idea is a draw from a Pareto distribution, and the draw represents the efficiency of producing the good by the technology just discovered. Using the stock of knowledge to represent the parameter of the Poisson process that characterizes the arrival in time of ideas does capture the effect of cumulative knowledge gained from R&D activities. However, this aggregate variable is not capable of capturing the impact of information externalities. To formalize the information externalities in a rigorous manner, we need to descend to a more disaggregate level and model how the findings from the R&D activities of one research organization can have a positive impact on the R&D activities of other research organizations. The objective of our paper is to fill part of this lacuna in the literature.

To fix ideas, and also to rigorously formalize the concept of information externalities, we have chosen to model R&D activities as the process of searching for a drug to treat a disease, with R&D activities being modelled from the perspective of the theory of optimal search and where the search is being conducted on chemical compounds housed in distinct chemical libraries. The main reason for formulating the R&D process in the context of the pharmaceutical industry is because much knowledge has been gained in the process of drug discovery, and this allows for a less abstract modeling of the R&D process.

In the model we formulate, it is a given that several brands of a drug are available at any instant for treating a single disease, and that pharmaceutical firms are carrying out R&D activities to find a new drug to treat the disease. It is assumed that the patent on each brand is held by a single pharmaceutical firm, and that after the patent for a brand has expired, the brand can be manufactured as a generic drug by a competitive fringe. Furthermore, pharmaceutical firms behave strategically both in the product market and in R&D. Under this structure, three scenarios are discussed: the first scenario refers to the case where all chemical compounds in all chemical libraries are already screened. The second scenario discusses the case where the set of unscreened chemical compounds include only one element. Under this scenario it is shown that the firm which holds the earlier-expiring patent only chooses to screen the last compound, when the patent it holds expires, if the expected discounted payoff net of R&D costs yielded by this action is positive. The expected discounted payoff net of R&D costs obtained by this firm is then decreasing in the cost of screening; increasing in the cumulative quality discovered in the past screenings of the compounds in the chemical library, and decreasing in the number of past screenings carried out in this chemical library. The payoff is also higher if the marginal cost of the drug manufactured from the last compound is lower, and higher if the qualities (marginal costs) of all the other brands – generic drugs as well as the brands whose patents have not expired – are lower (higher). It is also shown that if the firm which holds the earlier-expiring patent chooses not to screen the last compound when the patent it holds expires, the firm which holds the patent on the rival brand will not choose to screen the last compound when its patent expires. The expected discounted payoff earned by the rival brand is shown to be decreasing in the cumulative quality discovered in the chemical library, and increasing in the number of past

screenings in the chemical library; increasing (decreasing) in the quality (marginal cost) of the brand and decreasing (increasing) in the qualities (marginal costs) of the generic drugs as well as the brand whose patent has not expired.

The third scenario refers to the case where the set of unscreened chemical compounds includes two elements. These elements may be located in two different chemical libraries, or both being located in the same chemical library. Under the first case the analysis suggests that if neither compound is screened by the firm which holds the earlier-expiring patent when it stands alone as the single remaining compound, then it will not be screened either by this firm when it is one of the two remaining compounds. It is also shown that the expected discounted payoff net of R&D costs that the firm which holds the earlier-expiring patent obtains by screening each of the last two compounds is positive, then, every other thing equal, the compound with the lower screening cost should be screened first, the compound from which a new drug with much higher marginal cost is manufactured should not be screened first, and the compound with the potential quality that is stochastically much larger should be screened first. When the elements are both located in the same chemical library the penultimate compound in the chemical library is screened by the firm which holds the earlier-expiring patent, and if the revealed quality of the penultimate compound, is particularly high, then the probability that the quality of the last compound in the chemical library is higher than the quality of the penultimate compound is particularly low, which means the last compound will not be screened.

Drug discovery is a long and arduous process.[4] A pharmaceutical company employs thousands of researchers to find new drugs that can help people with various diseases. In spite of all the progress made in science and technology, drug discovery is still a lengthy and costly process. In 2000 the global R&D investment was $US 55 billion.[5] On average it takes up to 15 years to develop and test a new drug, and the required investments might rise to $US 600 million.

[4] Our account of drug discovery is based upon the article "ISOA/ARF Drug Development Tutorial," by Jens Eckstein found at http://www.alzforum.org/drg/tut/ISOATutorial.pdf **and** the article "Drug discovery," by Citizendium found at http://en.citizendium.org/wiki/Drug_discovery.
[5] See Toully *et al*. (2002).

In the past, drugs were discovered either by identifying active ingredients in traditional remedies or by serendipity. In the new paradigm of drug discovery, researchers first try to understand how a disease is controlled at the molecular and physiological levels. The knowledge gained at this stage helps identify a target, which is the specific cellular or molecular structure involved in the pathology. Next, through a process known as high-throughput screening (HTS) large libraries of chemicals are tested for their ability to modify the target. It is estimated that only about 1 in 5000 chemicals thus tested results in a lead. Through miniaturization and robotics, it is now possible to screen millions of compounds against targets in a very short period of time. Central to the new paradigm of drug discovery is the explosion of computational techniques that help analyze enormous volumes of data, prioritize HTS hits, and guide lead optimization. If a pharmaceutical company decides to develop a lead into a drug, the drug thus developed must go through a series of clinical trials before it can be approved by the authorities. In order for a drug to be approved it must exhibit therapeutic effects against the target and prove non-toxic to the patient.

Novel chemical structures (new drugs) can be found among natural products or from libraries of synthetic compounds created by combinatorial chemistry.[6] The vast majority of traditionally used crude drugs in Western medicine come from roots, leaves, and flowers of plants, and a pool of information about the potential of plant species – as a source of novel chemical structure – has been accumulated. The knowledge gained from ethno-botany can prove to be valuable in narrowing down the search for novel chemical structures among plants. Microbes compete for living space and food. The chemical structures that they have developed to compete against other species – because they have been tested and proved to be effective in their struggles for survival – can be sources of new drugs. Recently, some novel chemical structures have been found among marine invertebrates.

A guiding principle in the search for a novel chemical structure is the concept of chemical diversity,[7] which represents the current knowledge concerning the distribution of chemical

[6] In the past, chemists traditionally synthesized one compound at a time. With the modern technique of combinatorial chemistry, a large number of structurally distinct molecules can be synthesized at a time, and then submitted for pharmacological assay.

[7] Chemical diversity is an important concept in the discipline known as chemo-informatics, which is the application of informatics methods to solve chemical problems. Chemo-informatics involves the study of chemical information or molecular similarity and the development of computational methods for the identification and optimization of

compounds – based on their physicochemical characteristics – in the chemical space. An efficient search strategy, which tells us where to search for a novel chemical structure at any point in time, whether to continue or stop the search, or whether to go to another source to search for the desired novel chemical structure should exploit our knowledge concerning the chemical diversity of the various sources. Furthermore, because R&D in the pharmaceutical industry is profit-driven, the search for a novel chemical structure also depends on economics – search costs, production costs, competition from rival firms, and the appropriability of the discoveries.

The paper is organized as follows. In Section 2, the model, which is a dynamic model in continuous time, is presented. In conventional models of patent design, only one brand – the brand with the highest quality – is available on the market at any time. Furthermore, demand is completely inelastic: each consumer, regardless of income and regardless of the price of the brand offered on the market, buys exactly one unit of the brand. In the model we formulate, several differentiated products – the products whose patents are still in force and the products whose patents have expired – are available at any time on the market. Furthermore, the demand for a brand depends on income, its own price, and the prices of the other brands. In our model, the pharmaceutical firms with an active drug discovery program behave strategically in both R&D and in the product market. The model also contains a competitive fringe, which manufactures the brands whose patents have expired. In Section 3, some comparative static results concerning the impact of the cost and the quality of newly discovered drugs on the market are presented. The analysis of R&D is presented in Section 4. Some concluding remarks are given in Section 5.

2 The Model

Time is continuous, and is denoted by $t, t \geq 0$. The model deals with the case of a single disease, and in the model there are I pharmaceutical firms indexed by $i, i = 1, \ldots, I,$ where I is a positive integer, with $I \geq 2$. Each of these firms has an active R&D program to find a new drug for

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active compounds to the design of smart chemical databases and comprehensive computational infrastructures for interdisciplinary pharmaceutical research.

treating the disease. There is also a competitive fringe, which produces generic drugs, using the technical information disclosed in the patent of a brand after the patent on the brand has expired.

2.1 The R&D Process

The elucidation of the structure of a chemical compound serves to avoid the rediscovery of a chemical agent that is already known for its structure and chemical activities. A chemical compound can be identified by its mass/charge ratio after ionization with the help of mass spectrometry. The technique known as nuclear magnetic resonance (NMR) can be used to obtain information about individual atoms of a compound, which allows for a detailed reconstruction of the architecture of the compound. Most software used to address the chemical diversity of a population of compounds describe each compound in the population by its molecular fingerprint, which is a bit-string consisting of 0's and 1's that represent the answers to yes-no questions about the existence or absence of sub-structural features in the molecular structure of the compound in question.[8] Molecular fingerprints typically consist of hundreds, or even thousands, of bits. Thus, a 1000-bit fingerprint is a point in a 1000-dimensional chemical space. The Tanimoto dissimilarity index, which is $1 - the\ Tanimoto\ simlarity\ index,$ is often used to express the dissimilarity, or the distance,[9] between two compounds in a chemical space. In such a chemical space, similar compounds are expected to be located close to each other, while dissimilar compounds are located far apart. A much handier way to describe a compound is the BCUT[10] approach, which represents a compound as a point in a 6-dimensional Euclidean space. Adopting the philosophy of the BCUT approach, we shall characterize a chemical compound as a point in a low-dimensional Euclidean space, and the Euclidean distance between two compounds in such a chemical space can then be taken as how dissimilar they are as far as their chemical structures are concerned.

The search for a novel chemical structure to treat the disease in question is conducted among J sources, or libraries of chemical compounds, where J is a positive integer, with $J \geq 2$. For example, the search for a novel chemical structure might be conducted among plants (one

[8] Our account of representing a compound in the chemical space is based on Pearlman (2009).
[9] This distance is non-Euclidean.
[10] Pearlman, op cit.

source) or in the world of bacteria (another source). For each $j = 1, \dots, J$, let $X_j = \{x_{j,1}, \dots, x_{j,N_j}\}$ represent the set of chemical compounds – assumed to be distinct – that are housed in the jth library, with N_j being the number of compounds this library contains. Let $|x_{j,n} - x_{j',n'}|$ denote the Euclidean distance between two compounds $x_{j,n}$ and $x_{j',n'}$ in the chemical space. If the two compounds are distinct, then their distance is positive, and the more dissimilar they are the greater will be their distance.

In what follows, we shall assume that the effectiveness of a compound, say $x_{j,n}$, in treating the disease in question can be represented by an index, say $q_{j,n}$, that we call the quality of the chemical compound. The ordered pair $(x_{j,n}, q_{j,n})$ will be referred to as a drug. Before a drug can be manufactured, investments must be made to construct a production plant. To concentrate on the R&D activities carried out by the firms, we choose to ignore capital investments, and simply assume that after a drug, say $(x_{j,n}, q_{j,n})$, has been discovered, any volume of the drug can be manufactured at a constant marginal cost, say $c_{j,n}$. The list $(x_{j,n}, q_{j,n}, c_{j,n})$ will be referred to as a brand of the drug used to treat the disease in question. Note that for two brands, say $(x_{j,n}, q_{j,n}, c_{j,n})$ and $(x_{j',n'}, q_{j',n'}, c_{j',n'})$, if $x_{j,n} = x_{j',n'}$, then it is necessary that $q_{j,n} = q_{j',n'}$ and $c_{j,n} = c_{j',n'}$.

Consider a brand, say $(x_{j,n}, q_{j,n}, c_{j,n})$. Obviously, both $q_{j,n}$ and $c_{j,n}$ depend on $x_{j,n}$. For our purpose, we shall assume that the location of $x_{j,n}$ in the chemical space is known and that $c_{j,n}$, the marginal cost of manufacturing this compound to treat the disease in question is also known. As far as the value of $q_{j,n}$ is concerned, it is not known before the compound is screened, and thus can only be represented by a probability distribution that depends on the existing stock of knowledge.

Conceptually, we can characterize the qualities of the chemical compounds in a library, say the jth source, by a cumulative distribution function on $(q_{j,1}, \dots, q_{j,N_j})$, conditioned on $(x_{j,1}, \dots, x_{j,N_j})$. However, because of the enormous number of compounds in a chemical library, and because of the lack of knowledge on the potential of these compounds, it is extremely

difficult to postulate such a distribution function for each source. Furthermore, given that a large number – about 5000 to be a little more specific – of compounds must be screened before a lead is found, we shall assume that at any point in time all the compounds in a source that have not been screened have the same potential in the following sense. First, within each source, the cost for screening a compound is the same from one compound to the next. We shall let $\gamma_j, j = 1, \dots, J,$ denote the cost of screening a compound in the jth source. Second, within each source, say $j,$ the random variables $q_{j,1}, \dots, q_{j,N_j}$ are independently and identically distributed. These assumptions imply that the order in which the compounds in a source are screened is immaterial. Hence, we can assume that the compounds in a source are screened sequentially in the increasing order. Also, to concentrate on the information externalities of the R&D process, we shall ignore its time-consuming nature, and make the simplifying assumption that the time it takes to screen a compound against a target is negligible.

We can model $q_{j,n}, j = 1, \dots, J, n = 1, \dots, N_j,$ either as a continuous or a discrete random variable. For analytical convenience as well as for intuitive economic interpretation, we choose to model $q_{j,n}$ as a discrete random variable. More specifically, for each $j = 1, \dots, J,$ the potential qualities $q_{j,1}, \dots, q_{j,N_j}$ are Poisson random variables with parameter $\lambda_j,$ i.e., their common probability mass function is given by

$$f[q_{j,n}|\lambda_j] = \frac{\lambda_j^{q_{j,n}}}{(q_{j,n})!} e^{-\lambda_j}, \; q_{j,n} = 0,1, \dots, \qquad (n = 1, \dots, N_j).$$

Observe that $e^{-\lambda_j}$ represents the probability that a compound in source j has zero quality (completely ineffective in treating the disease). The Poisson process has been used by researchers, such as Arrow and Chang (1982), Chow (1981), Quyen (1991), and Cairns and Quyen (1998) to model discoveries in mineral exploration.

To model learning and the information externalities generated in the search for new drugs, we follow Quyen (1991) and adopt the approach of Bayesian statistical decision theory. Thus, for each $j = 1, \dots, J,$ we postulate a prior density for $\lambda_j,$ and then revise it repeatedly via the Bayes

formula, using the most recent data available on screening. We assume that at the beginning λ_j has a gamma distribution with parameters α_j and β_j, say

$$g_{\alpha_j,\beta_j}[\lambda_j] = \frac{1}{\Gamma(\alpha_j)\beta_j^{\alpha_j}} e^{-\lambda_j/\beta_j} {\lambda_j}^{\alpha_j - 1}, \lambda_j > 0.$$

In the statistical literature, the gamma density is known as a conjugate distribution of the Poisson process. The choice of a conjugate prior, in addition to making the computations much simpler, allows one to begin with a certain functional form for the prior and end up with a posterior of the same functional form, with the parameters updated by the sample information. Indeed, let

$$f_{\alpha_j,\beta_j}[q_{j,n}] = \int_0^\infty f[q_{j,n}|\lambda_j] g_{\alpha_j,\beta_j}[\lambda_j] d\lambda_j\,, \; q_{j,n} = 0,1,\ldots, \qquad (n = 1,\ldots,N_j).$$

be the marginal density of $q_{j,n}$, given the parameters (α_j, β_j) that characterize the prior density of λ_j. The conditional density of λ_j, given $q_{j,n}$, is

$$(1) \qquad f[\lambda_j|q_{,n}] = \frac{g_{\alpha_j,\beta_j}[\lambda_j] f[q_{j,n}|\lambda_j]}{f_{\alpha_j,\beta_j}[q_{j,n}]} = \frac{e^{-\frac{\lambda_j}{\beta_j}} {\lambda_j}^{\alpha_j - 1} e^{-\lambda_j} \lambda_j^{q_{j,n}}}{\Gamma[\alpha_j]\beta_j^{\alpha_j}[q_{j,n}]! f_{\alpha_j,\beta_j}[q_{j,n}]}$$

$$= g_{\alpha_j',\beta_j'}[\lambda_j] \frac{\Gamma[\alpha_j + q_{j,n}] \left(\frac{1}{1 + 1/\beta_j}\right)^{\alpha_j + q_{j,n}}}{\Gamma[\alpha_j]\beta_j^{\alpha_j}[q_{j,n}]!\, f_{\alpha_j,\beta_j}[q_{j,n}]},$$

where $g_{\alpha_j',\beta_j'}[\lambda_j]$ is the gamma density with parameters $\alpha_j' = \alpha_j + q, \beta_j' = \frac{1}{1+\frac{1}{\beta_j}}$.

Integrating (1) with respect to λ_j from 0 to ∞, we obtain

$$(2) \qquad \frac{\Gamma[\alpha_j + q_{j,n}] \left(\frac{1}{1+1/\beta_j}\right)^{\alpha_j + q_{j,n}}}{\Gamma[\alpha_j]\beta_j^{\alpha_j}[q_{j,n}]! f_{\alpha_j,\beta_j}[q_{j,n}]} = 1$$

Using (2) in (1), we see immediately that $f(\lambda_j|q_{j,n}) = g_{\alpha_j',\beta_j'}(\lambda_j)$, i.e., $g_{\alpha_j',\beta_j'}(\lambda_j)$ is the posterior density of λ_j, given $q_{j,n}$. Also, note that (2) can be rewritten as

$$(3) \qquad f_{\alpha_j,\beta_j}[q_{j,n}] = \frac{\Gamma[\alpha_j + q_{j,n}] \left(\frac{1}{1+1/\beta_j}\right)^{\alpha_j + q_{j,n}}}{\Gamma[\alpha_j]\beta_j^{\alpha_j}[q_{j,n}]!}, \; q_{j,n} = 0,1,\ldots, \qquad (n = 1,\ldots,N_j).$$

which is the marginal density of $q_{j,n}$, given the parameters (α_j, β_j) of the prior density of λ_j. The distribution function associated with $f_{\alpha_j,\beta_j}[q_{j,n}]$ is

(4) $F_{\alpha_j,\beta_j}[q] = \sum_{q'=0}^{q} f_{\alpha_j,\beta_j}[q'],$ $(q = 0,1, \dots.)$

The following lemma, due to Quyen (1991), gives some useful properties of $F_{\alpha_j,\beta_j}[q]$.

LEMMA 1: *The distribution function F_{α_j,β_j} is stochastically increasing in each of the parameters α_j and β_j. More precisely, for each given value of $q, q = 0,1, \dots$, we have the following results:*

(i) *For each given β_j, the map $\alpha_j \to F_{\alpha_j,\beta_j}[q]$ is strictly decreasing. Furthermore, $\ell im_{\alpha_j \to \infty} F_{\alpha_j,\beta_j}[q] = 0$.*

(ii) *For each given α_j, the map $\beta_j \to F_{\alpha_j,\beta_j}(q)$ is strictly decreasing. Furthermore, $\ell im_{\beta_j \to 0} F_{\alpha_j,\beta_j}[q] = 1$.*

Before any compound in a source, say X_j, is screened, the potential quality of a typical compound in this source is believed to be Poisson with parameters λ_j, which in turn has a prior density that is gamma with parameters (α_j, β_j). The probability mass function $f_{\alpha_j,\beta_j}[q], n = 1, \dots, n_j$, as represented by (3), characterizes the quality of a typical compound in X_j. Now suppose that the first compound, namely $x_{j,1}$, is screened for its potential as a new drug to treat the disease in question, and the screening reveals that its quality is $q_{j,1}$. The number of compounds in X_j that remain to be screened is now $n_j - 1$, and the uncertain quality of a typical remaining compound is believed to be Poisson with parameter λ_j, which in turn is gamma with updated parameters $\alpha_j' = \alpha_j + q_{j,1}$ and $\beta_j' = \frac{1}{1+\frac{1}{\beta_j}}$. In particular, the probability mass function that characterizes the quality of a typical remaining compound is $f_{\alpha_j',\beta_j'}[q_{j,n}], n = 2, \dots, N_j$. Note that the higher is the revealed quality of the compound $x_{j,1}$ after it has been screened against the target, the more optimistic our beliefs will be concerning the potential of a typical remaining compound in source X_j. If n compounds in X_j have been screened and the qualities of these

compounds have been revealed as $q_{j,1}, \dots, q_{j,n}$, then the potential quality of a typical remaining compound is embodied in the distribution function $F_{\alpha_j'[n],\beta_j'[n]}[q]$, where we have let $\alpha_j'[1] = \alpha_j, \beta_j'[1] = \beta_j$, and for each $k = 1, \dots, n$, we have let $\alpha_j'[k+1] = \alpha_j'[k] + q_{j,k}$, $\beta_j'[k+1] = 1/(1 + 1/\beta_j'[k])$. In view of Lemma 1.(i), the higher is the sum $q_{j,1} + \cdots + q_{j,n}$ of the revealed qualities, the more favourable will be the potential quality of a typical remaining compound, and this is economically quite intuitive: the more successful is the search for a new drug in a chemical library, the higher will be the potential quality of a typical remaining compound in this chemical library.

At the beginning, if we interpret α_j and $\frac{1}{\beta_j}$, respectively, as the *cumulative quality* revealed and *the number of compounds screened* in the past, then $\alpha_j'[n]$ and $1/\beta_j'[n]$ represent, respectively, the cumulative revealed quality and the number of compounds that have been screened – past and present – after n more compounds have been screened. The list $\big((x_{j,1}, q_{j,1}, c_{j,1}), \dots, (x_{j,n}, q_{j,n}, c_{j,n})\big)$ represents the history of the search in X_j, and the ordered pair $\big(\alpha_j'[n], \beta_j'[n]\big)$ embodies all the learning from the R&D activities of all the firms in the industry if the information generated in their search programs is pooled.

2.2 Patent Breadth

As far as the granting of a patent is concerned, how novel a new drug is obviously depends on its distance from the patented brand in the chemical space. Furthermore, it is also reasonable to consider a new drug as not infringing on a patented brand if it comes from a source that is different from the source from which the patented brand is manufactured. Pig insulin, cow insulin, and human insulin produced by bacteria are all various brands of insulin used to treat diabetics. Insulin can be produced from plants[11] or fungi.[12] Recently, Symbiosis,[13] a Calgary-based company, claimed to have developed a technology for producing insulin from the safflower at a cost of 40% lower than that of traditional processes, and that the insulin produced

[11] "Commercial Production of Insulin and Insulin-lke Proteins in Plants," United States Patent 7393998.
[12] "Process for the Production of Insulin by Genetically Transformed Fungal Cells," United States Patent 408 2613.
[13] http://www.DefeatDiabetes.org.

from the safflower is virtually indistinguishable from human insulin. Insulin produced from the safflower thus does not infringe on the patent on human insulin produced by bacteria according to the recombinant DNA technology. Thus, for patent purposes, the distance – or novelty – between two brands, say $(x_{j,n}, q_{j,n}, c_{j,n})$ and $\left(x_{j\prime,n\prime}, q_{j\prime,n\prime}, c_{j',n\prime}\right)$, can be defined in the following manner

$$(5) \quad d\left(\left(x_{j,n}, q_{j,n}, c_{j,n}\right), \left(x_{j',n'}, q_{j',n'}, c_{j',n'}\right)\right) = \epsilon_1 \left|x_{j,} - x_{j',n'}\right| + \epsilon_2 \left|q_{j,n} - q_{j',n'}\right| + \epsilon_3 \left|c_{j,n} - c_{j',n'}\right| + \delta_{jj'},$$

where $\epsilon_1, \epsilon_2, \epsilon_3$ are positive parameters strictly smaller than 1, and $\delta_{jj\prime} = 1$ if $j \neq j'$, $\delta_{jj\prime} = 0$ if $j = j'$. Note that the distance between two brands, as defined by (5) is a weighted sum of (i) their distance in the chemical space, (ii) their quality differential, (iii) their cost differential, and (iv) $\delta_{jj\prime}$ a distance between two sources, with the distance being assigned the value 1 if they are distinct and the value 0 if they are the same. Note that the distance defined by (5) captures both product innovation – the first, second, and fourth term on the right-hand side of (5) – and process innovation – the third term on the right-hand side of (5).

Using the distance between two brands, as represented by (5), we can define the breadth – or more precisely, the leading breadth – of a patent as a number $B, 0 < B < 1$, such that a new brand, say $\left(x_{j\prime,n\prime}, q_{j\prime,n\prime}, c_{j',n\prime}\right)$, is judged not to infringe on a patented brand, say $\left(x_{j,n}, q_{j,n}, c_{j,n}\right)$, if $q_{j\prime,n\prime} \geq q_{j,n}$ and $d\left(\left(x_{j,n}, q_{j,n}, c_{j,n}\right), \left(x_{j\prime,n\prime}, q_{j\prime,n\prime}, c_{j',n\prime}\right)\right) > B$. In the literature on patent design, another concept of patent breadth – lagging breadth – is also proposed. The difference between the two concepts of breadth is that the leading breadth protects the patented product from the competition by superior products, while the lagging breadth protects the patented product from the competition by inferior products. An immediate implication of the adoption of a leading breadth is that the quality of the most recently patented brand rises through time. For a more detailed analysis of these two concepts of patent breadth, the reader can consult O'Donoghue *et al.*, op cit.

We have characterized a brand as a list $\left(x_{j,n}, q_{j,n}, c_{j,n}\right)$, which describes, respectively, its location in the chemical space, its quality in treating the disease in question, and its marginal cost (the

cost of manufacturing one unit of this chemical compound). For economic considerations, it is also necessary to add another dimension to the characterization of a brand: the date on which the brand is patented. Thus, we shall from now on represent a brand by a list, $\omega = (x_{j,n}, q_{j,n}, c_{j,n}, \tau_{j,n})$, where $\tau_{j,n}$ is the date on which the brand is patented. Also, we let L denote the length of a patent.

2.3 Preferences

For each $t \geq 0$, let $\Omega[t]$ denote the set of brands that are available on the market at time t. The set $\Omega[t]$ consists of the brands whose patents have expired and are now manufactured by the fringe as well as the brands whose patents are still in force. In what follows, we shall denote by $\Omega^{-}[t]$ the totality of brands whose patents have expired by time t. Because a generic drug must compete against the leading brands and against the other generic drugs, not all the brands whose patents have expired will be marketed by the fringe. Thus, only those brands in $\Omega^{-}[t]$ with a sufficiently low production cost and a sufficiently high quality will be marketed by the fringe. However, without any loss of generality we can assume that $\Omega^{-}[t]$ is a subset of $\Omega[t]$ by interpreting an element of $\Omega^{-}[t]$ that is not marketed as a generic drug that the fringe is willing to supply, but there is no demand for it due to its high price or low quality. Note that the set $\Omega^{-}[t]$ gets larger with time as more and more brands whose patents have expired are added to it.

The representative consumer consumes a numéraire good and various brands of the drug available on the market, and her preferences are represented by the following Cobb-Douglas utility function:

(6) $$u\left(y_0, (y_\omega)_{\omega \epsilon \Omega[t]}\right) = y_0^{1-\eta}\left(e^{\sum_{\omega \epsilon \Omega[t]} Log[q_{j,n} y_\omega + 1]}\right)^{\eta}.$$

In (6), $0 < \eta < 1$, is a parameter, y_0 is the consumption of the numéraire good, and y_ω is the consumption of the brand $\omega = (x_{j,n}, q_{j,n}, c_{j,n}, \tau_{j,n}) \epsilon \Omega[t]$.

The representative consumer chooses the consumption bundle $\left(y_0, (y_\omega)_{\omega \epsilon \Omega[t]}\right)$ that maximizes (6) subject to the following budget constraint:

(7) $y_0 + \sum_{\omega \epsilon \Omega[t]} p_\omega y_\omega = m[t].$

In (7), p_ω denotes the price of the brand ω.

If we interpret the quality of a drug as its therapeutic contents, then $\overline{y}_\omega = q_{j,n} y_\omega$ represents the effective consumption of the brand ω. Let $\overline{p}_\omega = p_\omega / q_{j,n}$ and $\overline{c}_{j,n} = c_{j,n}/q_{j,n}$ denote, respectively, the price and the marginal cost – normalized by its own quality – of the brand ω. As defined, $\overline{p}_\omega$ and $\overline{c}_{j,n}$ represent, respectively, the price and the marginal cost of effective consumption. In what follows, we will simply refer to $\overline{p}_\omega$ and $\overline{c}_{j,n}$ as the effective price and the effective marginal cost of the brand ω, respectively. Adopting the interpretation of quality as the therapeutic contents of a drug, we can restate the problem faced by the representative consumer under the following simpler form:

(8) $max_{\left(y_0, (\overline{y}_\omega)_{\omega \epsilon \Omega[t]}\right)} y_0^{1-\eta} \left(e^{\sum_{\omega \epsilon \Omega[t]} Log[\overline{y}_\omega + 1]}\right)^\eta$

subject to

(9) $y_0 + \sum_{\omega \epsilon \Omega[t]} \overline{p}_\omega \overline{y}_\omega = m[t].$

This is a simple utility maximization problem whose solution is given by

(10) $$\begin{aligned} \overline{y}_\omega &= \frac{\eta}{1-\eta+\eta|\Omega[t]|} \frac{m[t] + \sum_{\omega' \epsilon \Omega[t]} \overline{p}_{\omega'}}{\overline{p}_\omega} - 1 \\ &= \frac{\eta}{1-\eta+\eta|\Omega[t]|} \left(\frac{m[t] + \sum_{\omega' \epsilon (\Omega[t]-\omega)} \overline{p}_{\omega'}}{\overline{p}_\omega} + 1 \right) - 1 \\ &= \frac{\eta}{1-\eta+\eta|\Omega[t]|} \left(\frac{m[t] + \sum_{\omega' \epsilon (\Omega[t]-\omega)} \overline{p}_{\omega'}}{\overline{p}_\omega} \right) - \left(1 - \frac{\eta}{1-\eta+\eta|\Omega[t]|} \right) \\ &= \frac{\eta}{1-\eta+\eta|\Omega[t]|} \left(\frac{m[t] + \sum_{\omega' \epsilon (\Omega[t]-\omega)} \overline{p}_{\omega'}}{\overline{p}_\omega} \right) - \frac{1-2\eta+\eta|\Omega[t]|}{1-\eta+\eta|\Omega[t]|} \\ &= \frac{\kappa_1 m_\omega[t]}{\overline{p}_\omega} - \kappa_0, \qquad (\omega \epsilon \Omega[t]). \end{aligned}$$

where $|\Omega[t]|$ denotes the number of elements of $\Omega[t]$, and

(11) $m_\omega[t] = m[t] + \sum_{\omega' \epsilon (\Omega[t]-\omega)} \overline{p}_{\omega'}$,

(12) $\kappa_0 = \frac{1-2+\eta|\Omega[t]|}{1-\eta+\eta|\Omega[t]|}, \kappa_1 = \frac{\eta}{1-\eta+\eta|\Omega[t]|}$.

3 The Prices of Drugs

In practice, a pharmaceutical firm might market several brands of the drug at any time. However, to keep the exposition from becoming overburdened with notations, we shall make the simplifying assumption that if a pharmaceutical firm chooses to market a certain brand of the drug that it has patented, then it will market this brand exclusively during the statutory life of the patent on this brand. Because once the patent on a brand has expired, it will be marketed as a generic drug by the competitive fringe at cost, the firm that held the patent on the brand will not make any profit by continuing to market this brand. Thus, we shall assume that when this happens, the firm will stop marketing the brand, and must search for a new brand of the drug if it wishes to stay in the market. For the brands whose patents have not yet expired, their prices will be strategically set by the holders of these patents. To study the strategic behaviour of these firms, we shall consider the simple case in which the set of brands whose patents have not yet expired at time t consists of only two brands, say $\omega' = (x_{j',n'}, q_{j',n'}, c_{j',n'}, \tau_{j',n'})$ and $\omega'' = (x_{j'',n''}, q_{j'',n''}, c_{j'',n''}, \tau_{j'',n''})$, and that these two brands are held by two different firms. Analyzing the case of more than two pharmaceutical firms that are active in the search for a new drug will force us to consider the numerous combinations of dates on which the drugs discovered by these firms are patented. While this adds more realism to the model, it does not yield any more insights into the R&D process. Also, for simplicity we consider in this section the simple case of a single generic drug, say $\omega = (x_{j,n}, q_{j,n}, c_{j,n}, \tau_{j,n})$, which is manufactured and sold by the fringe at production cost, i.e., $\overline{p}_{\omega} = \overline{c}_{j,n}$. The generalization to the case of more than one generic drug on the market can be made in a straightforward manner.

Let $\overline{p}_{\omega'}$ $(\overline{p}_{\omega''}, resp.)$ denote the effective price of the brand ω' $(\omega'', resp.)$ set at time t by the firm which holds the patent on this brand. The profit earned at time t by the brand ω' is

(13) $$(\overline{p}_{\omega'} - \overline{c}_{j',n'}) \left(\kappa_1 \frac{m_{\omega'}[t]}{\overline{p}_{\omega'}} - \kappa_0 \right).$$

Maximization of (13) with respect to $\overline{p}_{\omega'}$ we obtain the following reaction function for the firm that holds the patent on the brand ω':

(14) $\phi_{\omega\prime}: \overline{p}_{\omega\prime\prime} \to \overline{p}_{\omega\prime} = \frac{\sqrt{\kappa_1}\sqrt{m[t]+\overline{p}_{\omega\prime\prime}+\overline{c}_{j,n}}\sqrt{\overline{c}_{j\prime,n\prime}}}{\sqrt{\kappa_0}}$.

Note that $\phi_{\omega\prime}$ is strictly increasing and strictly concave, and that its slope tends to 0 when $\overline{p}_{\omega\prime\prime} \to \infty$.

Similarly, we obtain the following reaction function for the firm that holds the patent on the brand ω'':

(15) $\phi_{\omega\prime\prime}: \overline{p}_{\omega\prime} \to \overline{p}_{\omega\prime\prime} = \frac{\sqrt{\kappa_1}\sqrt{m[t]+\overline{p}_{\omega\prime}+\overline{c}_{j,n}}\sqrt{\overline{c}_{j\prime\prime,n\prime\prime}}}{\sqrt{\kappa_0}}$.

Like the reaction curve $\phi_{\omega\prime}$, the reaction curve $\phi_{\omega\prime\prime}$ is also strictly increasing, strictly concave, and its slope (with respect to the $\overline{p}_{\omega\prime}$ price axis) approaches 0 when $\overline{p}_{\omega\prime} \to \infty$. The reaction curves of the two firms are depicted in Figure 6.

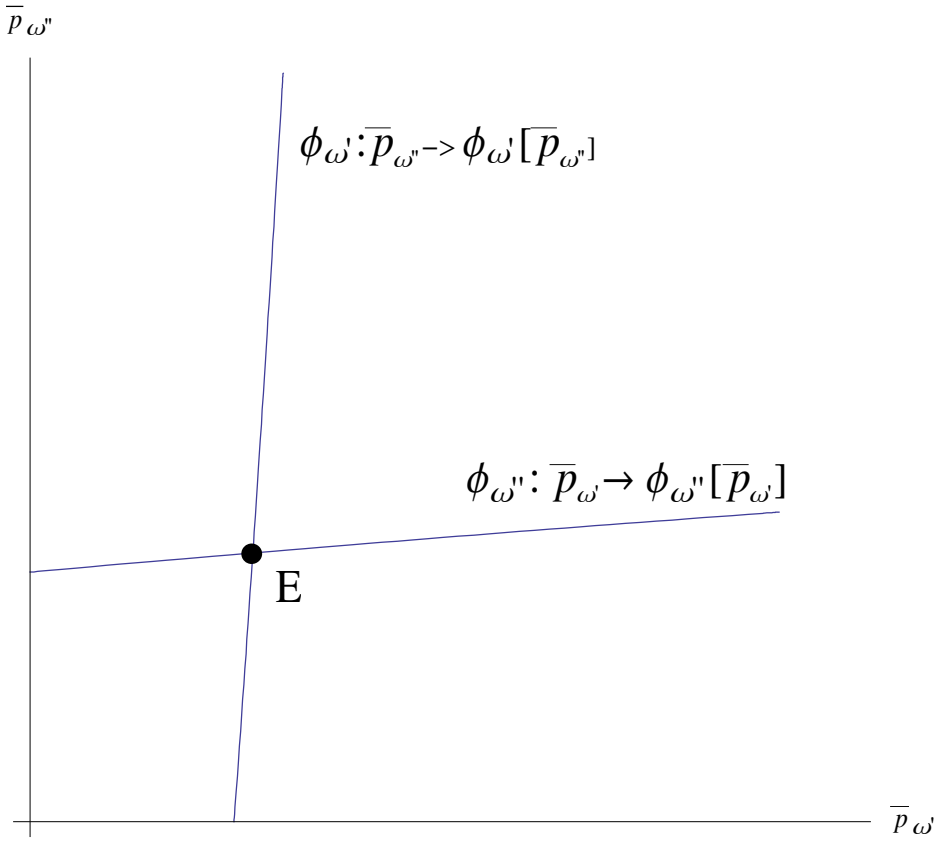

Figure 6. The equilibrium effective prices of drugs

The two reaction curves intersect at a unique point, which is depicted as point E in Figure 6 and which represents the effective prices set by the two firms under the equilibrium at each instant.

An alternative – and more effective – way for finding the equilibrium prices and for carrying out comparative static exercises is through the two composite maps

(16) $$\Phi_{\omega\prime}:\overline{p}_{\omega\prime} \to \phi_{\omega'}[\phi_{\omega''}[\overline{p}_{\omega'}]] = \frac{1}{\sqrt{\kappa_0}}\sqrt{\kappa_1}\sqrt{\bar{c}_{j',n'}}\sqrt{m[t] + \bar{c}_{j,n} + \frac{\sqrt{\kappa_1}\sqrt{m[t]+\overline{p}_{\omega\prime}+\bar{c}_{j,n}}\sqrt{\bar{c}_{j'',n''}}}{\sqrt{\kappa_0}}},$$

and

(17) $$\Phi_{\omega\prime\prime}:\overline{p}_{\omega\prime\prime} \to \phi_{\omega\prime\prime}\left[\phi_{\omega'}[\overline{p}_{\omega''}]\right] = \frac{1}{\sqrt{\kappa_0}}\sqrt{\kappa_1}\sqrt{\bar{c}_{j'',n''}}\sqrt{m[t] + \bar{c}_{j,n} + \frac{\sqrt{\kappa_1}\sqrt{m[t]+\overline{p}_{\omega\prime\prime}+\bar{c}_{j,n}}\sqrt{\bar{c}_{j',n'}}}{\sqrt{\kappa_0}}}.$$

The curve depicting the composite map $\Phi_{\omega\prime}$ is depicted in Figure 7. It begins at $\overline{p}_{\omega\prime} = 0$ above the 45-degree line. It is strictly increasing, strictly concave, and its slope approaches 0 when

$\overline{p}_{\omega'} \to \infty$. Hence the curve crosses the 45-degree line at a unique point, which represents the equilibrium effective price of the brand ω'. In the same manner, the unique fixed point of the composite map $\Phi_{\omega''}$ represents the equilibrium effective price of the brand ω''.

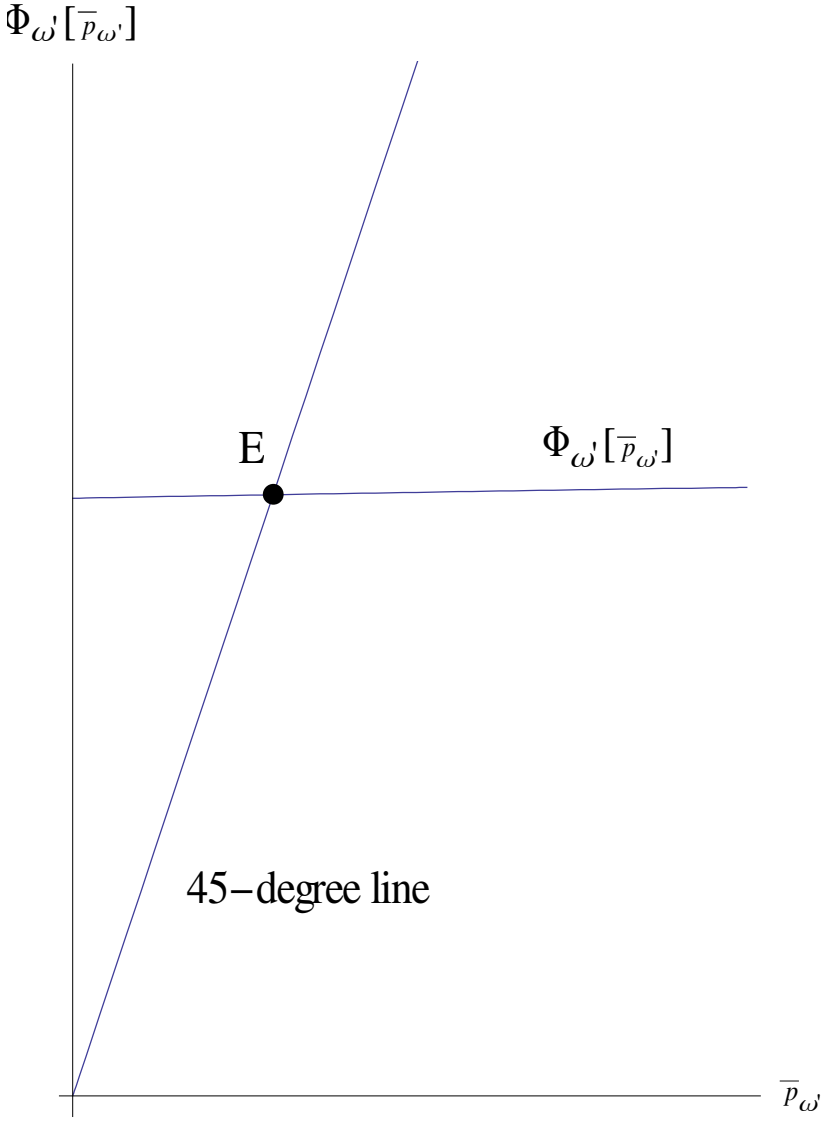

Figure 7. The composite map $\Phi_{\omega'}[\overline{p}_{\omega'}] = \phi_{\omega'}[\phi_{\omega''}[\overline{p}_{\omega'}]]$

In what follows, the market share of a brand is defined as the revenue it earns relative to the total revenues earned by the industry. The following proposition gives the comparative static results of a variation in the effective marginal cost of a brand marketed by a firm that holds the patent on this brand.

PROPOSITION 1: *For a brand whose patent has not expired, the higher is its effective marginal cost,*

(i) *the higher will be its effective price, the lower will be its market share, and the lower will be the profits it earns;*

(ii) *the higher will be the effective price, the market share, and the profits of the rival brand;*

(iii) *the higher will be the total revenues and market share of generic drugs.*

PROOF: The proof of Proposition 1 is given in Annex A.

The following proposition describes how the quality and the prices of generic drugs influence the pricing behaviour of the firms that hold the patents currently in force.

PROPOSITION 2: *The higher is the effective cost of the generic drugs,*

(i) *the lower will be their revenues and their market share;*

(ii) *the higher will be the effective price, the output, the market share, and the profits of each of the brands whose patents has not expired.*

PROOF: The proof of Proposition 2 is given in Annex B.

In what follows, we shall let $v_{\omega\prime}[t, m[t], \omega', \omega'', \Omega^{-}[t]]$ and $v_{\omega\prime\prime}[t, m[t], \omega', \omega'', \Omega^{-}[t]]$ denote the profit earned at time t by the brand ω' and the brand ω'', respectively.

4 R&D and Information Externalities

In this section, as in Section 3.3, we shall assume that in the industry there are two firms each of which has an active drug discovery program and a competitive fringe, which markets the brands whose patents have expired as generic drugs. Also, we shall assume that the income of the representative consumer is not varying over time; that is, $m[t] = m = constant$.

In a drug discovery program, a pharmaceutical firm has to decide which compound in which chemical library to screen as well as the timing of the screening. To concentrate on the information generated in the R&D activities of the pharmaceutical firms and to keep the model from becoming too complex, we shall eschew the modeling of the timing of the screenings as a strategic decision variable, and shall make two simplifying assumptions on R&D. First, a pharmaceutical firm with an active drug discovery program will only screen a chemical compound to find a new drug when the patent on the brand it currently markets expires. Second, if a pharmaceutical firm chooses not to carry out any screening when the patent on the brand it currently markets expires, it will terminate all R&D activities and exit the market. With these simplifying assumptions, the only strategic decision a pharmaceutical firm needs to consider is the chemical library and the compound in that chemical library to concentrate its efforts on. To study the evolution of technological progress in the pharmaceutical industry, we try to find the sub-game perfect Nash equilibrium of the dynamic game played by the firms in this industry. The sub-game perfect Nash equilibrium is found by backward induction on the set of chemical compounds not yet screened.

If all the compounds in all the chemical libraries have been screened, there is nothing left to discuss as far R&D is concerned, and all that needs to be done is to analyze the strategic behaviour in the product market of the holders of the patents on the brands which have not yet expired. This task was carried out in Section 3.3. So, we begin the backward induction with the case in which the set of chemical compounds that have not been screened contains only one element.

4.1 One Remaining Unscreened Chemical Compound

Suppose that among all the chemical libraries there remains only a compound that has not been screened, say the compound $(x_{j,N_j}, q_{j,N_j}, c_{j,N_j})$, which is the last compound in the jth chemical library. Also, suppose that the information obtained from the past screenings in this chemical library leads us to believe that the potential quality of this chemical compound is represented by the probability mass function $f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]$.

Let $\omega' = (x_{j',n'}, q_{j',n'}, c_{j',n'}, \tau_{j',n'})$ and $\omega'' = (x_{j'',n''}, q_{j'',n''}, c_{j'',n''}, \tau_{j'',n''})$ be the two brands currently marketed by the two pharmaceutical firms that hold the patents on these brands. Without any loss of generality, we assume that $\tau'' < \tau'$. That is, the patent on the brand ω'' was granted before that on the brand ω', and thus the patent on the former brand will expire before the patent on the latter brand. According to the assumption that a pharmaceutical firm will only carry out the screenings needed to find a new drug when the patent it holds on the brand it currently markets expires, the last chemical compound will be screened by the firm which holds the patent on the brand ω'' if this firm finds the screening to be profitable.

If the pharmaceutical firm which holds the patent on the brand ω'' chooses to screen the last compound, then the newly discovered drug can only be patented if its quality is at least equal to the quality of the brand that is most recently patented, namely the brand ω', and if its distance from ω' is greater than the breadth that protects the brand ω'; that is, if q_{j,N_j} belongs to the set

(18) $Q_{j,N_j}[\omega'] = \left\{ q_{j,N_j} \middle| q_{j,N_j} \geq q_{j',n'}, d\left((x_{j',n'}, q_{j',n'}, c_{j',n'}), (x_{j,Nj}, q_{j,N_j}, c_{j,N_j})\right) > B \right\}.$

In this case, the discounted value – discounted to the time the patent on the brand ω'' expires – of the stream of profits earned by the newly discovered drug is given by

(19) $$A_1[q_{j,N_j}] = \int_{\tau_{j'',n''}+L}^{\tau_{j',n'}+L} e^{-r\left(s-\tau_{j'',n''}-L\right)} v_{\omega^-}\left[s, m, \omega^-, \omega', \Omega^-[s]\right] ds + \int_{\tau_{j',n'}+L}^{\tau_{j'',n''}+2L} e^{-r(s-\tau_{j'',n''}-L)} v_{\omega^-}\left[s, m, \omega^-, \Omega^-[s]\right] ds.$$

In (19), r is the market rate of interest, and $\omega^- = \left(x_{j,N_j}, q_{j,N_j}, c_{j,N_j}, \tau_{j,N_j}\right)$ represents the newly discovered drug, with $\tau_{j,N_j} = \tau_{j'',n''} + L$ as the date on which the last compound is screened, which is also the date on which the newly discovered drug is patented. Also, $\Omega^-[s]$, we recall, represents the set of brands whose patents have expired by time s.

The first integral in (19) represents the discounted value of the stream of profits earned by the newly discovered drug from the time of its discovery until the time the patent on the brand ω' expires. During the time interval $\left[\tau_{j'',n''}+L, \tau_{j',n'}+L\right)$, the newly discovered drug has to compete against the brand ω' marketed by the rival pharmaceutical firm which holds the patent on this brand as well as against all the generic drugs – which include its own predecessor (the brand ω'') and all the brands whose patents expired by time $\tau_{j'',n''}+L$. Under the integral sign, the expression $v_{\omega}\text{-}\left[s, m, \omega^{-}, \omega', \Omega^{-}[s]\right]$ represents the profit earned by the newly discovered drug at each time s during the time interval $\left[\tau_{j'',n''}+L, \tau_{j',n'}+L\right)$. According to Proposition 1, $v_{\omega}\text{-}\left[s, m, \omega^{-}, \omega', \Omega^{-}[s]\right]$ is strictly increasing (decreasing) in the marginal cost (quality) of the rival brand ω'. According to Proposition 2, $v_{\omega}\text{-}\left[s, m, \omega^{-}, \omega', \Omega^{-}[s]\right]$ is strictly decreasing (increasing) in the quality (marginal cost) of each generic drug.

The second integral in (19) represents the discounted value of the stream of profits earned by the newly discovered drug from time $\tau_{j',n'}+L$ until the end of its statutory life. During this time interval, the newly discovered drug only faces competition from the generic drugs, which include the brand ω' whose patent expired at time $\tau_{j',n'}+L$. The expression $v_{\omega}\text{-}\left[s, m, \omega^{-}, \Omega^{-}[s]\right]$ under the integral sign represents the profit earned by the newly discovered drug at each time s during the time interval $\left[\tau_{j',n'}+L, \tau_{j'',n''}+2L\right)$. Note that $v_{\omega}\text{-}\left[s, m, \omega^{-}, \Omega^{-}[s]\right]$ is strictly decreasing (increasing) in the quality (marginal cost) of each generic drug.

According to Proposition 1, $A_1[q_{j,N_j}]$ is strictly increasing in q_{j,N_j}. It is also higher if the quality (marginal cost) of the brand ω' is lower (higher). According to Proposition 2, $A_1[q_{j,N_j}]$ is higher if qualities (marginal costs) of the generic drugs are lower (higher).

Under the event that the screening of the compound $(x_{j,N_j}, q_{j,N_j}, c_{j,N_j})$ does not yield any patentable drug, the firm that holds the patent on the brand ω'' incurred the R&D cost γ_j without obtaining any benefits.

The discounted value of the stream of profits earned by the firm which holds the patent on the brand ω'' if it chooses to screen the last compound when this patent expires – as a function of the quality of this compound – is then given by

(20) $A_2[q_{j,N_j}] = \begin{cases} A_1[q_{j,N_j}]\ if\ q_{j,N_j} \in Q_{j,N_j}[\omega'], \\ 0, otherwise. \end{cases}$

From the discussion on the properties of $A_1[q_{j,N_j}]$, we can assert that $A_2[q_{j,N_j}]$ is increasing (decreasing) in q_{j,N_j} $(c_{j,n})$. It is decreasing (increasing) in the qualities (marginal costs) of all the other brands – those whose patents have expired and those whose patents have not expired. The expected discounted profit net of R&D costs – with the discounting being carried back to the time the patent on the brand ω'' expires – that the firm which holds this patent obtains from by screening the last compound is then given by

(21) $A_3 = -\gamma_j + \sum_{q_{j,N_j} \geq 0} A_2[q_{j,N_j}] f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]$.

Let

(22)

$$V_{\omega''}\left[\omega', \omega'', \Omega^{-}[\tau_{j'',n''} + L]\left[\left(x_{j,N_j}, q_{j,N_j}, c_{j,N_j}\right), f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]\right]\right] = max\{0, A_3\}.$$

denote the expected discounted payoff net of R&D cost – discounted to the time the patent on the brand ω'' expires – that the firm which holds the patent on the brand ω'' obtains, given that (i) the patent on the brand ω'' was granted before the patent on the rival brand ω', and (ii) the probability mass function which characterizes the quality of the last compound is $f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]$.

PROPOSITION 3: *The firm which holds the patent on the brand ω'' only chooses to screen the last compound when the patent it holds on the brand ω'' expires if $A_3 > 0$, i.e., if the expected discounted payoff net of R&D costs yielded by this action is positive. Furthermore, if this is the case, then the expected discounted payoff net of R&D costs obtained by this firm is*

(i) *decreasing in γ_j, the cost of screening;*

(ii) *increasing in $\alpha_j[N_j]$, the cumulative quality discovered in the past screenings of the compounds in the jth chemical library, and decreasing in $\frac{1}{\beta_j[N_j]}$, the number of past screenings carried out in this chemical library;*

(iii) *decreasing in the marginal cost of the drug manufactured from the last compound.*

(iv) *decreasing (increasing) in the qualities (marginal costs) of all the other brands – generic drugs as well as the brands whose patents have not expired.*

PROOF: The proof of Proposition 3 is given in Annex C.

LEMMA 2: *If the firm which holds the patent on the brand ω'' chooses not to screen the last compound when the patent it holds on the brand ω'' expires, then neither will the firm which holds the patent on the rival brand ω' choose to screen the last compound when this patent expires.*

PROOF: The proof of Lemma 2 is given in Annex D.

Now let

(23) $$V_{\omega'}\left[\omega', \omega'', \Omega^{-}[\tau_{j''n''} + L]\left[\left(x_{j,N_j}, q_{j,N_j}, c_{j,N_j}\right), f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]\right]\right.$$

denote the expected discounted payoff – discounted to the time the patent on the brand ω'' expires – that the firm which holds the patent on the brand ω' obtains, given that (i) the patent on the brand ω'' was granted before the patent on the rival brand ω', and (ii) the probability mass function which characterizes the quality of the last compound is $f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]$. This expected discounted payoff can be computed as follows.

If the firm which holds the patent on the brand ω'' chooses to screen the last compound and obtains a patentable drug ω^{-} from the screening, then the discounted value – discounted to the

time the patent on the brand ω'' expires – of the stream of profits earned by the brand ω' from time $\tau_{j'',n''} + L$ until the end of its statutory life is

(24) $A_4[q_{j,N_j}] = \int_{\tau_{j'',n''}+L}^{\tau_{j',n'}+L} e^{-r\left(s-\tau_{j'',n''}-L\right)} v_{\omega'}[s, m, \omega^-, \omega', \Omega^-[s]]ds.$

On the other hand, under the event that the firm which holds the patent on the brand ω'' fails to obtain a patentable drug from screening the last compound, the discounted value – discounted to the time the patent on the brand ω'' expires – of the stream of profits earned by the brand ω' from time $\tau_{j'',n''} + L$ until the end of its statutory life is

(25) $A_5 = \int_{\tau_{j'',n''}+L}^{\tau_{j',n'}+L} e^{-r\left(s-\tau_{j'',n''}-L\right)} v_{\omega'}[s, m, \omega', \Omega^-[s]]ds.$

Thus, if the firm which holds the patent on the brand ω'' chooses to screen the last chemical compound when the patent on the brand ω'' expires, then the expected discounted value of the stream of profits earned by the brand ω' from time $\tau_{j'',n''} + L$ until the end of its statutory life – with the discounting being carried back to the time the patent on the brand ω'' expires – is given by

(26) $A_6 = \sum_{q_{j,N_j} \in Q_{j,N_j}[\omega']} A_4[q_{j,N_j}] f_{(\alpha_j[N_j],\beta_j[N_j])}\left[q_{j,N_j}\right]$
$+A_5\left(1 - \sum_{q_{j,N_j} \epsilon Q_{j,N_j}[\omega']} f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]\right).$

If the firm which holds the patent on the brand ω'' chooses not to screen the last chemical compound, then according to Lemma 2, the last compound will not be screened by the firm which holds the patent on the brand ω' either, when the patent on the brand ω' expires. Under this scenario, the expected discounted value – discounted to the time the patent on the brand ω'' expires – of the stream of profits earned by the brand ω' is also given by A_5.

We are now ready to give the explicit expression for (23) as follows:

(27) $V_{\omega'}\left[\omega', \omega'', \Omega^-[\tau_{j'',n''} + L]\left[\left(x_{j,N_j}, q_{j,N_j}, c_{j,N_j}\right), f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]\right]\right] =$

$$\begin{cases} A_6 \text{ if the firm which holds the patent on the brand } \omega'' \text{screens the last compound,} \\ A_5 \text{ if the firm which holds the patent on the brand } \omega'' \text{does not screen the last compound.} \end{cases}$$

PROPOSITION 4: *The expected discounted payoff – discounted to the time the patent on the brand* ω'' *expires – that is earned by the firm which holds the patent on the brand* ω' *from time* $\tau_{j'',n''} + L$ *until the end of the statutory life of the patent on the brand* ω' *is*

(i) *decreasing in* $\alpha_j[N_j]$*, the cumulative quality discovered in the* j*th chemical library, and increasing in* $\frac{1}{\beta_j[N_j]}$*, the number of past screenings in the* j*th chemical library;*

(ii) *increasing (decreasing) in the quality (marginal cost) of the brand* ω'

(iii) *decreasing (increasing) in the qualities (marginal costs) of the generic drugs as well as the brands whose patents have not expired.*

PROOF: The proof of Proposition 4 is given in Annex E.

4.2 Two Remaining Unscreened Chemical Compounds

Let $\omega' = (x_{j',n'}, q_{j',n'}, c_{j',n'}, \tau_{j',n'})$ and $\omega'' = (x_{j'',n''}, q_{j'',n''}, c_{j'',n''}, \tau_{j'',n''})$, with $\tau'' < \tau'$, be the two brands currently marketed by the two pharmaceutical firms which hold the patents on these brands. Suppose that there remain only two chemical compounds that have not been screened, say $\left(x_{j[\ell],n[\ell]}, q_{j[\ell],n[\ell]}, c_{j[\ell],n[\ell]}\right), \ell = 1,2$. There are two possibilities to consider: (i) the two compounds are located in two different chemical libraries, and (ii) the two compounds are located in the same chemical library. Under the first possibility, screening one compound yields only information about this compound, but no information about the other compound. Under the second possibility, screening the penultimate compound yields information about this compound and information about the last compound.

4.2.1 The Two Chemical Compounds are Located in Two Different Chemical Libraries

Suppose that the last two compounds that have not been screened are located in two different chemical libraries. Under this scenario, each compound is the last one in a chemical library, i.e.,

$$\left(x_{j[\ell],n[\ell]}, q_{j[\ell],n[\ell]}, c_{j[\ell],n[\ell]}\right) = \left(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}\right), \qquad (\ell = 1,2),$$

with $j[1] \neq j[2]$. Also, suppose that the qualities of these compounds are characterized by the probability mass functions $f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}], \ell = 1,2$.

For each $\ell = 1,2$, let

(28) $A_7^{\ell} = V_{\omega,,}\left[\omega', \omega'', \Omega^{-}\left[\tau_{j''},_{n,,} + L\right] \middle| (x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}), f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]\right]$

denote the expected discounted payoff net of R&D costs that the firm which holds the patent on the brand ω'' obtains under the assumption that $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ stands alone as the single remaining compound, not as one of the two remaining compounds.

LEMMA 3:

(i) *If $A_7^{\ell} \leq 0, \ell = 1,2$,* i.e., *if neither compound is screened by the firm which holds the patent on the brand ω'' when it stands alone as the single remaining compound, then it will not be screened, either, by this firm when it is one of the two remaining compounds. The same result holds for the firm which holds the patent on the brand ω' when this patent expires.*

(ii) *If $A_7^{\ell} > 0, A_7^{\ell'} \leq 0$, then the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ will be screened by the firm which holds the patent on the brand ω'' when this patent expires. Furthermore, regardless of the outcome of the screening, the compound $(x_{j[\ell']},_{N_{j[\ell']}}, q_{j[\ell']},_{N_{j[\ell']}}, c_{j[\ell']},_{N_{j[\ell']}})$ will not be screened by the firm which holds the patent on the brand ω' when this patent expires.*

PROOF: The proof of Lemma 3 is given in Annex F.

If $A_7^{\ell} > 0, \ell = 1,2$, then neither compound can be summarily rejected, and the question concerning the order in which the compounds are screened arises.

Suppose that the firm which holds the patent on the brand ω'' chooses to screen the compound $\left(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}\right)$ immediately after the patent on the brand ω'' has expired. Under the event that the screening leads to a patentable drug, i.e., if $q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega']$, where

(29) $$Q_{j[\ell],N_{j[\ell]}}[\omega'] = \left\{q_{j[\ell],N_{j[\ell]}} \middle| q_{j[\ell],N_{j[\ell]}} \geq q_{j',n'}, d((x_{j',n'}, q_{j',n'}, c_{j',n'}), (x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})) > B\right\},$$

then the discounted value – discounted to time the patent on the brand ω'' expires – of the stream of profits earned by the newly discovered drug during the time interval $[\tau_{j'',n''} + L, \tau_{j',n'} + L)$ is given by

(30) $$A_8^{\ell}\left[q_{j[\ell],N_{j[\ell]}}\right] = \int_{\tau_{j'',n''}+L}^{\tau_{j',n'}+L} e^{-r(s-\tau_{j'',n''}-L)} v_{\omega^{\ell}}\left[s, m, \omega^{\ell}, \omega', \Omega^{-}[s]\right] ds,$$

where $\omega^{\ell} = \left(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}, \tau_{j[\ell],N_{j[\ell]}}\right)$, with $\tau_{j[\ell],N_{j[\ell]}} = \tau_{j'',n''} + L$, denotes the newly discovered drug. Furthermore, at time $\tau_{j',n'} + L$, when the patent on the brand ω' expires, the two pharmaceutical firms find themselves exactly in the situation analyzed in Sub-section 3.4.1, but with their roles reversed. Now there is only one compound left for screening, namely the compound $\left(x_{j[\ell'],N_{j[\ell']}}, q_{j[\ell'],N_{j[\ell']}}, c_{j[\ell'],N_{j[\ell']}}\right), \ell' \neq \ell$, and the two brands marketed by the two pharmaceutical firms are ω^{ℓ} and ω', with the patent on the latter brand being granted before the patent on the former brand. Under such a scenario, the expected discounted payoff – discounted to the time the patent on the brand ω' expires – earned by the firm which holds the patent on the brand ω^{ℓ} after the patent on the brand ω' has expired is given by

(31) $$A_9^{\ell}[q_{j[\ell],N_{j[\ell]}}] = V_{\omega^{\ell}}\left[\omega^{\ell}, \omega', \Omega^{-}[\tau_{j',n'} + L] \middle| (x_{j[\ell'],N_{j[\ell']}}, q_{j[\ell'],N_{j[\ell']}}, c_{j[\ell'],N_{j[\ell']}}), f_{\left(\alpha_{j[\ell']}\left[N_{j[\ell']}\right], \beta_{j[\ell']}\left[N_{j[\ell']}\right]\right)}\left[q_{j[\ell'],N_{j[\ell']}}\right]\right].$$

The discounted payoff – discounted to the time the patent on the brand ω'' expires – earned by the firm which holds the patent on the brand ω'' under the event that the screening of the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ results in a patentable drug is then given by

(32) $$A_{10}^{\ell}[q_{j[\ell],N_{j[\ell]}}] = A_8^{\ell}[q_{j[\ell],N_{j[\ell]}}] + e^{-r(\tau_{j',n'}-\tau_{j'',n''})} A_9^{\ell}[q_{j[\ell],N_{j[\ell]}}].$$

On the other hand, if the screening of the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ is not fruitful, then the two firms also find themselves in the same situation analyzed in Sub-section 3.4.1, with $(x_{j[\ell']],N_{j[\ell']}}, q_{j[\ell']],N_{j[\ell']}}, c_{j[\ell']],N_{j[\ell']}})$ being the last remaining chemical compound. The expected discounted payoff – discounted to the instant the patent on the brand ω'' expires – that this firm earns after the first unsuccessful attempt is $A_7^{\ell'}$, according to (28).

If the first screening was not fruitful, and if $A_7^{\ell'} > 0$, then there will be a surge in R&D activities: the firm which holds the patent on the brand ω'' will continue the search by screening immediately the remaining compound, namely the compound $(x_{j[\ell']],N_{j[\ell']}}, q_{j[\ell']],N_{j[\ell']}}, c_{j[\ell']],N_{j[\ell']}})$. Under this scenario, $A_7^{\ell'}$ represents the discounted payoff net of R&D cost – discounted to the time the patent on the brand ω'' expires – that is yielded by the second screening.

The expected discounted payoff net of R&D costs – discounted to the time the patent on the brand ω'' expires – that the firm which holds the patent on the brand ω'' obtains by screening the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ is given by

(33) $$A_{11}^{\ell} = -\gamma_{j[\ell]} + \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega']} A_{10}^{\ell}[q_{j[\ell],N_{j[\ell]}}] f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]$$
$$+A_7^{\ell'}\left(1 - \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega']} f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]\right).$$

Obviously, if $A_{11}^{\ell} \leq 0$, then the ℓth remaining compound will not be screened by the firm which holds the patent on the brand ω'' when this patent expires. In particular, if $A_{11}^{\ell} \leq 0$, for each $\ell = 1,2$, then the firm which holds the patent on the brand ω'' will shut down its R&D activities and exit the market after the patent on the brand ω'' has expired.

When both A_{11}^{ℓ} and $A_{11}^{\ell'}$ are positive, it is necessary to compare them in order to find out which compound should be screened first. Because of the numerous parameters involved – the dates on which the patents on the brands ω' and ω'' were granted; the screening costs of the two remaining unscreened compounds; the potential qualities of these compounds; and the marginal costs of the drugs manufactured from these compounds – it is difficult to determine

unambiguously the sign of the payoff differential $A_{11}^{\ell} - A_{11}^{\ell\prime}$. Intuitively, we expect that the order of screening should favours the compound with lower screening cost and higher potential quality. It should also favour the compound from which a drug with a lower marginal cost could be discovered. The following proposition confirms our intuition of the influence of screening costs on the order of screening.

PROPOSITION 5: *Suppose that* $A_{11}^{\ell} > 0, \ell = 1,2$. *Then, every other thing equal, the compound with the lower screening cost should be screened first.*

PROOF: The proof of Proposition 5 is given in Annex G.

PROPOSITION 6: *Suppose that* $A_{11}^{\ell} > 0, \ell = 1,2$. *Every other thing equal, the compound from which a new drug with much higher marginal cost is manufactured should not be screened first.*

PROOF: The proof of Proposition 6 is given in Annex H.

PROPOSITION 7: *Suppose that* $A_{11}^{\ell} > 0, \ell = 1,2$. *Then every other thing equal, the compound with the potential quality that is stochastically much larger should be screened first.*

PROOF: The proof of Proposition 7 is given in Annex I.

Let

$$(34)\quad V_{\omega''}\left[\omega', \omega'', \Omega^{-}[\tau_{j'',n''} + L] \middle| \left((x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}), f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]\right)_{\ell=1}^{2}\right] = max\left\{0, \left(A_{11}^{\ell}\right)_{\ell=1}^{2}\right\}$$

denote the expected discounted payoff for the firm which holds the patent on the brand ω'', given that (i) the patent on the brand ω'' was granted before the patent on the brand ω', (ii) there are two remaining unscreened compounds, $\left((x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})\right)_{\ell=1}^{2}$, which are located in two different chemical libraries, and (iii) for each $\ell = 1,2$, the potential quality of the remaining

unscreened compound ℓ is represented by the probability mass function $f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]$.

Let

(35) $V_{\omega'}\left[\omega', \omega'', \Omega^{-}[\tau_{j'',n''}+L]\middle|\left((x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}), f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]\right)_{\ell=1}^{2}\right]$

denote the expected discounted payoff – discounted to the time the patent on the brand ω'' expires – for the firm which holds the patent on the brand ω', given that (i) the patent on the brand ω'' was granted before the patent on the brand ω', (ii) there are two remaining unscreened compounds, $\left((x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})\right)_{\ell=1}^{2}$, which are located in two different chemical libraries, and (iii) for each $\ell = 1,2$, the potential quality of the remaining unscreened compound ℓ is represented by the probability mass function $f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]$. This expected discounted payoff can be computed as follows.

First, if the firm which holds the patent on the brand ω'' chooses to screen the compound $\left(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}\right)$ immediately after the patent on the brand ω'' has expired, and if the screening results in a patentable drug $\omega^{\ell} = (x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}, \tau_{j[\ell],N_{j[\ell]}})$, with $\tau_{j[\ell],N_{j[\ell]}} = \tau_{j'',n''} + L$, then the expected discounted payoff – discounted to the time the patent on the brand ω'' expires – for the firm which holds the patent on the brand ω' is given by

(36) $A_{12}^{\ell}[q_{j[\ell],N_{j[\ell]}}] =$

$\int_{\tau_{j'',n''}+L}^{\tau_{j',n'}+L} e^{-r\left(s-\tau_{j'',n''}-L\right)} v_{\omega'}\left[s, m, \omega^{\ell}, \omega', \Omega^{-}[s]\right] ds + e^{-r(\tau_{j',n'}-\tau_{j'',n''})} \times V_{\omega'}\Big[\omega^{\ell}, \omega', \Omega^{-}[\tau_{j',n'}+$

$L]\Big|(x_{j[\ell\prime],N_{j[\ell\prime]}}, q_{j[\ell\prime],N_{j[\ell\prime]}}, c_{j[\ell\prime],N_{j[\ell\prime]}}), f_{(\alpha_{j[\ell\prime]}[N_{j[\ell\prime]}],\beta_{j[\ell\prime]}[N_{j[\ell\prime]}])}[q_{j[\ell\prime],N_{j[\ell\prime]}}]\Big]$.

In (44), $\Omega^{-}\left[\tau_{j',n'}+L\right] = \Omega^{-}[\tau_{j'',n''}+L] \cup \{\omega'\}$.

If the screening of the compound $\left(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}\right)$ is not fruitful, then immediately after this screening, we have the situation analyzed in Sub-section 3.4.1, and the expected discounted payoff – discounted to the time the patent on the brand ω'' expires – for the firm which holds the patent on the brand ω' is given by

(37) $A_{13}^{\ell\prime} =$

$V_{\omega\prime}\left[\omega', \omega'', \Omega^{-}[\tau_{j'',n''} + L]\,\middle|\,(x_{j[\ell\prime],N_{j[\ell\prime]}}, q_{j[\ell\prime],N_{j[\ell\prime]}}, c_{j[\ell\prime],N_{j[\ell\prime]}}), f_{(\alpha_{j[\ell\prime]}[N_{j[\ell\prime]}],\beta_{j[\ell\prime]}[N_{j[\ell\prime]}])}[q_{j[\ell\prime],N_{j[\ell\prime]}}]\right].$

Thus, under the scenario that the firm which holds the patent on the brand ω'' chooses to screen the compound $\left(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}\right)$ immediately after the patent on the brand ω'' has expired, then the expected discounted payoff – discounted to the time the patent on the brand ω'' expires – for the firm which holds the patent on the brand ω' is given by

(38) $A_{14}^{\ell} = \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega\prime]} A_{12}^{\ell}[q_{j[\ell],N_{j[\ell]}}] f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]$

$+\left((1 - \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega\prime]} f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}])\right) A_{13}^{\ell\prime}.$

Second, if the firm which holds the patent on the brand ω'' chooses not to carry out any screening when the patent it holds on the brand ω'' expires, then it will shut down its R&D activities and exit the market. Under this scenario, the discounted profit – discounted to the time the patent on the brand ω'' expires – earned by the brand ω' from time $\tau_{j'',n''} + L$ until time $\tau_{j',n\prime} + L$ is given by

(39) $A_{15} = \int_{\tau_{j'',n''}+L}^{\tau_{j',n\prime}+L} e^{-r\left(s-\tau_{j'',n''}-L\right)} v_{\omega\prime}[s, m, , \omega', \Omega^{-}[s]]ds.$

At time $\tau_{j',n\prime} + L$, when the patent it holds on the brand ω' expires, this firm might choose to screen one of the remaining compounds, say the compound $\left(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}\right)$. If the screening is fruitful and results in a patentable drug, say $\omega^{\ell} = \left(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}\right)$, then the expected discounted payoff – discounted to time $\tau_{j',n\prime} + L$ – obtained by this firm is given by

(40) $A_{16}^{\ell}[q_{j[\ell],N_{j[\ell]}}] = \int_{\tau_{j',n'}+L}^{\tau_{j',n'}+2L} e^{-r\left(s-\tau_{j',n'}-L\right)} v_{\omega^{\ell}}\left[s, m, \omega^{\ell}, \Omega^{-}[s]\right] ds + e^{-rL} \times$

$V_{\omega^{\ell}}\left[\Omega^{-}[\tau_{j',n'}+2L] \middle| (x_{j[\ell\prime],N_{j[\ell\prime]}}, q_{j[\ell\prime],N_{j[\ell\prime]}}, c_{j[\ell\prime],N_{j[\ell\prime]}}), f_{(\alpha_{j[\ell\prime]}[N_{j[\ell\prime]}],\beta_{j[\ell\prime]}[N_{j[\ell\prime]}])}[q_{j[\ell\prime],N_{j[\ell\prime]}}]\right].$

On the other hand, if the screening of the compound $\left(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}\right)$ is not fruitful, then the expected discounted payoff – discounted to time $\tau_{j',n'}+L$ – obtained by the firm after the patent on the brand ω' has expired is given by

(41) $A_{17}^{\ell\prime} = V_{\omega\prime}\left[\Omega^{-}[\tau_{j',n'}+L] \middle| (x_{j[\ell\prime],N_{j[\ell\prime]}}, q_{j[\ell\prime],N_{j[\ell\prime]}}, c_{j[\ell\prime],N_{j[\ell\prime]}}), f_{(\alpha_{j[\ell\prime]}[N_{j[\ell\prime]}],\beta_{j[\ell\prime]}[N_{j[\ell\prime]}])}[q_{j[\ell\prime],N_{j[\ell\prime]}}]\right].$

The expected discounted payoff – discounted to the time the patent on the brand ω' expires – earned by the firm which holds the patent on the brand ω' after this patent has expired, given that (i) the firm which holds the patent on the brand ω'' chooses not to carry out any screening when this patent expires, and (ii) the firm which holds the patent on the brand ω' chooses to screen the compound $\left(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}\right)$ when the patent on the brand ω' expires, is then given by

(42) $A_{18}^{\ell} = -\gamma_{j[\ell]} + \sum_{q_{j[\ell],N_{j[\ell]}} \epsilon Q_{j[\ell],N_{j[\ell]}}[\omega\prime]} A_{16}^{\ell}[q_{j[\ell],N_{j[\ell]}}] f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]$

$+\left(1 - \sum_{q_{j[\ell],N_{j[\ell]}} \epsilon Q_{j[\ell],N_{j[\ell]}}[\omega\prime]} f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]\right) A_{17}^{\ell\prime}.$

The expected discounted payoff – discounted to the time the patent on the brand ω'' expires – earned by the firm which holds the patent on the brand ω' after this patent has expired, given that (i) the firm which holds the patent on the brand ω'' chooses not to carry out any screening when this patent expires, and (ii) the firm which holds the patent on the brand ω' chooses to screen the compound $\left(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}\right)$ when the patent on the brand ω' expires, is then given by

(43) $A_{19} = A_{15} + e^{-r(\tau_{j',n\prime}-\tau_{j'',n''})} \max\{0, A_{18}^{\ell}, A_{18}^{\ell\prime}\}.$

We are now ready to give the explicit expression for (35) as

(44) $V_{\omega\prime}\left[\omega', \omega'', \Omega^{-}[\tau_{j'',n''}+L] \middle| \left((x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}), f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]\right)_{\ell=1}^{2}\right]$

$$= \begin{cases} A_{14}^{\ell} \; if \; the \; firm \; which \; holds \; the \; patent \; on \; the \; brand \; \omega'' chooses \; to \; screen \\ the \; compound \; \left(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}}\right) when \; the \; patent \; on \; the \; brand \; \omega'' expires, \\ A_{19} \; if the \; firm \; which \; holds \; the \; patent \; on \; the \; brand \; \omega'' chooses \; not \; to \; screen \; one \; of \\ the \; two \; remaining \; ompounds \; when \; the \; patent \; on \; the \; brand \; \omega'' expires. \end{cases}$$

4.2.2 The Two Remaining Compounds are Located in the Same Chemical Library

Suppose that the last two chemical compounds that have not been screened are both located in the $jth \; chemical \; library$, i.e., the two remaining compounds are $(x_{j,N_j-1}, q_{j,N_j-1}, c_{j,N_j-1})$ and $(x_{j,N_j}, q_{j,N_j}, c_{j,N_j})$. Furthermore, their uncertain qualities are characterized by the same probability mass function $f_{(\alpha_j[N_j-1],\beta_j[N_j-1])}[q_{j,N_j-1}]$. The firm which holds the patent on the brand ω'' has only two possible choices when this patent expires: to screen or not to screen.

Suppose that the firm which holds the patent on the brand ω'' chooses to screen the penultimate compound immediately when the patent on the brand ω'' expires, and that the screening results in a patentable drug, say $\omega^1 = (x_{j,N_j-1}, q_{j,N_j-1}, c_{j,N_j-1}, \tau_{j,N_j-1})$, with $\tau_{j,N_j-1} = \tau_{j'',n''} + L$, $q_{j,N_j-1} \in Q_{j,N_j-1}[\omega']$, where

(45) $Q_{j,N_j-1}[\omega'] =$

$$\left\{q_{j,N_j-1} \middle| q_{j,N_j-1} \geq q_{j',n'}, d((x_{j',n'}, q_{j',n'}, c_{j',n'}), (x_{j,N_j-1}, q_{j,N_j-1}, c_{j,N_j-1})) > B\right\}$$

then the discounted value – discounted to time the patent on the brand ω'' expires – of the stream of profits earned by the newly discovered drug during the time interval $[\tau_{j'',n''} + L, \tau_{j',n'} + L)$ is

(46) $\int_{\tau_{j'',n''}+L}^{\tau_{j',n'}+L} e^{-r(s-\tau_{j'',n''}-L)} v_{\omega^1}[s, m, \omega^1, \omega', \Omega^-[s]]ds,$

Furthermore, at time $\tau_{j',n'} + L$, when the patent on the brand ω' expires, the two pharmaceutical firms find themselves exactly in the situation analyzed in Sub-section 3.4.1, but with their roles reversed. Now there is only one compound left for screening, namely the compound $(x_{j,N_j}, q_{j,N_j}, c_{j,N_j})$, and the two brands marketed by the two pharmaceutical firms are ω' and ω^1, with the patent on the former brand being granted before that on the latter.

Furthermore, the probability mass function that characterizes the uncertain quality of the compound $(x_{j,N_j}, q_{j,N_j}, c_{j,N_j})$ is now revised – in light of the revealed quality of the penultimate compound – to be $f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]$. where $\alpha_j[N_j] = \alpha_j[N_j - 1] + q_{j,N_j-1}$ and $\frac{1}{\beta_j[N_j]} = 1 + \frac{1}{\beta_j[N_j-1]}$. Also, according to Lemma 1, the revised distribution that characterizes our beliefs concerning the uncertain quality of the last remaining compound is stochastically increasing in the quality of the newly discovered drug. Under such a scenario, the expected discounted payoff – discounted to the time the patent on the brand ω' expires – earned by the firm which holds the patent on the brand ω^1 after the patent on the brand ω' has expired is given by

(47) $A_{20}\left[q_{j,N_j-1}\right] = V_{\omega^1}\left[\omega^1, \omega', \Omega^-[\tau_{j',n'} + L]\,\middle|\,(x_{j,N_j}, q_{j,N_j}, c_{j,N_j}), f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]\right]$.

The discounted payoff – discounted to the time the patent on the brand ω'' expires – earned by the firm which holds the patent on the brand ω'' under the event that the screening of the compound $(x_{j,N_j-1}, q_{j,N_j-1}, c_{j,N_j-1})$ results in a patentable drug is then given by

(48) $A_{21}\left[q_{j,N_j-1}\right] = \int_{\tau_{j'',n''}+L}^{\tau_{j',n'}+L} e^{-r\left(s-\tau_{j'',n''}-L\right)} v_{\omega^1}[s, m, \omega^1, \omega', \Omega^-[s]]ds + e^{-r(\tau_{j',n'}-\tau_{j'',n''})} A_{20}[q_{j,N_j-1}]$.

On the other hand, if the screening of the compound $(x_{j,N_j-1}, q_{j,N_j-1}, c_{j,N_j-1})$ is not fruitful, then the two firms also find themselves in the same situation analyzed in Sub-section 3.4.1, with $(x_{j,N_j}, q_{j,N_j}, c_{j,N_j})$ being the last chemical compound. Under this event, this firm might give up, or it might screen the last compound immediately after the first unsuccessful attempt. The expected discounted payoff – discounted to the instant the patent on the brand ω'' expires – that this firm earns after the first unsuccessful attempt is

(49) $A_{22}[q_{j,N_j-1}] = V_{\omega''}\left[\omega', \omega'', \Omega^-[\tau_{j'',n''} + L]\,\middle|\,(x_{j,N_j}, q_{j,N_j}, c_{j,N_j}), f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]\right]$.

If the first screening was not fruitful, and if $A_{22}[q_{j,N_j-1}] > 0$, then this firm will continue the search by screening the remaining compound, namely the compound $(x_{j,N_j}, q_{j,N_j}, c_{j,N_j})$ immediately, and under this scenario, (49) represents the discounted payoff net of R&D cost –

discounted to the time the patent on the brand ω'' expires – that is yielded by the second screening.

The expected discounted profit net of R&D cost made by the firm which holds the patent on the brand ω'' – discounted to the time this patent expires – if this firm chooses to screen the penultimate compound immediately after the patent on the brand ω'' expires is then given by

(50) $$A_{23} = -\gamma_j + \sum_{q_{j,N_j-1} \in Q_{j,N_j-1}[\omega']} A_{21}[q_{j,N_j-1}] f_{(\alpha_j[N_j-1],\beta_j[N_j-1])}[q_{j,N_j-1}] + \left(1 - \sum_{q_{j,N_j-1} \in Q_{j,N_j-1}[\omega']} f_{(\alpha_j[N_j-1],\beta_j[N_j-1])}[q_{j,N_j-1}]\right) A_{22}[q_{j,N_j-1}]$$

Let

(51) $$V_{\omega''}\left[\omega', \omega'', \Omega^{-}[\tau_{j'',n''} + L] \middle| \left((x_{j,n}, q_{j,n}, c_{j,n})\right)_{n=N_j-1}^{N_j}, f_{(\alpha_j[N_j-1],\beta_j[N_j-1])}\left[q_{j,N_j-1}\right]\right] = max\{0, A_{23}\}$$

denote the expected discounted payoff – discounted to the time the patent on the brand ω'' expires – for the firm which holds this patent, given that the remaining two compounds are the last two compounds in the $jth\ chemical\ library$ and that the uncertain quality of each of these two compounds is characterized by the common probability mass function $f_{(\alpha_j[N_j-1],\beta_j[N_j-1])}[q_{j,N_j-1}]$. The firm which holds the patent on the brand ω'' will only carry out the screening if this expected payoff is positive.

The information generated from the screening of the penultimate compound in the $jth\ chemical\ library$ resolves not only the quality of this compound, but it also yields information about the potential quality of the last compound. The information thus obtained on the potential quality of the last compound will have a bearing on the decision whether or not this compound will be screened. According to Lemma 1, if the screening of the penultimate compound is not particularly fruitful, then expectations concerning the potential quality of the last compound will be much lowered, and this compound might never be screened, especially when there are many brands competing for a limited amount of drug expenditures. On the other hand, if the screening of the penultimate compound is fruitful, then the potential quality of the

last compound will also be stochastically larger. However, this does not necessarily mean that the last compound will be screened for a possible new drug. Indeed, if the screening of the penultimate compound is particularly fruitful, then no efforts will be expended in screening the last compound, as asserted by the following proposition:

PROPOSITION 8: *Suppose that the penultimate compound in the* $jth\ chemical\ library$ *is screened by the firm which holds the patent on the brand* ω'' *when this patent expires. If* q_{j,N_j-1}, *the revealed quality of the penultimate compound, is particularly high, then the probability that the quality of the last compound in the* $jth\ chemical\ library$ *is higher than* q_{j,N_j-1} *– so that the drug developed from the last compound can be patented – is particularly low, and this means that the last compound will not be screened.*

PROOF: The proof and a numerical example in support of Proposition 8 is given in Annex J.

Let

(52) $$V_{\omega'}\left[\omega', \omega'', \Omega^{-}[\tau_{j'',n''} + L] \middle| \left((x_{j,n}, q_{j,n}, c_{j,n})\right)_{n=N_j-1}^{N_j}, f_{(\alpha_j[N_j-1],\beta_j[N_j-1])}[q_{j,N_j-1}]\right]$$

denote the expected discounted payoff – discounted to the time the patent on the brand ω'' expires – for the firm which holds the patent on the brand ω', given that the remaining two compounds are the last two compounds in the $jth\ chemical\ library$ and that the uncertain quality of each of these two compounds is characterized by the common probability mass function $f_{(\alpha_j[N_j-1],\beta_j[N_j-1])}[q_{j,N_j-1}]$. This expected discounted payoff can be computed as follows.

First, if the firm which holds the patent on the brand ω'' chooses to screen the compound $(x_{j,N_j-1}, q_{j,N_j-1}, c_{j,N_j-1})$ immediately after the patent on the brand ω'' has expired, and if the screening results in a patentable drug, say $\omega^1 = (x_{j,N_j-1}, q_{j,N_j-1}, c_{j,N_j-1}, \tau_{j,N_j-1})$, with $\tau_{j,N_j-1} = \tau_{j'',n''} + L$, then the expected discounted payoff – discounted to the time the patent on the brand ω'' expires – for the firm that holds the patent on the brand ω' is given by

(53) $A_{24} = \int_{\tau_{j'',n''}+L}^{\tau_{j',n'}+L} e^{-r\left(s-\tau_{j'',n''}-L\right)} v_{\omega'}\left[s, m, \omega^1, \omega', \Omega^-[s]\right] ds + e^{-r(\tau_{j',n'}-\tau_{j'',n''})} \times$

$$V_{\omega'}\left[\, \omega^1, \omega', \Omega^-[\tau_{j',n'}+L] \,\middle|\, (x_{j,N_j}, q_{j,N_j}, c_{j,N_j}), f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]\right].$$

In (53), $\Omega^-\left[\tau_{j',n'}+L\right] = \Omega^-[\tau_{j'',n''}+L] \cup \{\omega'\}$.

If the screening of the compound $(x_{j,N_j-1}, q_{j,N_j-1}, c_{j,N_j-1})$ is a failure, then immediately after this screening, we have the situation analyzed in Sub-section 3.4.1, and the expected discounted payoff – discounted to the time the patent on the brand ω'' expires – for the firm which holds the patent on the brand ω' is given by

(54) $A_{25} = V_{\omega'}\left[\, \omega', \omega'', \Omega^-[\tau_{j'',n''}+L] \,\middle|\, (x_{j,N_j}, q_{j,N_j}, c_{j,N_j}), f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]\right].$

Thus, under the scenario that the firm which holds the patent on the brand ω'' chooses to screen the compound $(x_{j,N_j-1}, q_{j,N_j-1}, c_{j,N_j-1})$ immediately after the patent on the brand ω'' has expired, then the expected discounted payoff – discounted to the time the patent on the brand ω'' expires – for the firm which holds the patent on the brand ω' is given by

(55) $A_{26} = \sum_{q_{j,N_j-1} \in Q_{j,N_j-1}[\omega']} A_{24} f_{(\alpha_j[N_j-1],\beta_j[N_j-1])}[q_{j,N_j-1}]$

$$+ \left(1 - \sum_{q_{j,N_j-1} \in Q_{j,N_j-1}[\omega']} f_{(\alpha_j[N_j-1],\beta_j[N_j-1])}[q_{j,N_j-1}]\right) A_{25}.$$

Second, if the firm which holds the patent on the brand ω'' chooses not to carry out any screening when the patent on the brand ω'' expires, then the expected discounted profit – discounted to the time the patent on the brand ω'' expires – earned by the brand ω' from time $\tau_{j'',n''}+L$ until time $\tau_{j',n'}+L$ is given by

(56) $A_{27} = \int_{\tau_{j'',n''}+L}^{\tau_{j',n'}+L} e^{-r\left(s-\tau_{j'',n''}-L\right)} v_{\omega'}\left[s, m, \omega', \Omega^-[s]\right] ds.$

Furthermore, the firm which holds the patent on the brand ω' is the only one left in the R&D sector. At time $\tau_{j',n'}+L$, when the patent on the brand ω' expires, this firm might choose not to screen one of the two remaining compounds, and the game ends at time $\tau_{j',n'}+L$. On the other

hand if it chooses to screen the penultimate compound, and obtains a patentable drug, say $\omega^1 = \left(x_{j,N_j-1}, q_{j,N_j-1}, c_{j,N_j-1}, \tau_{j,N_j-1}\right)$, with $\tau_{j,N_j-1} = \tau_{j',n'} + L$, then the expected discounted payoff – discounted to time $\tau_{j',n'} + L$ – obtained by this firm is given by

$$(57)\quad A_{28} = \int_{\tau_{j',n'}+L}^{\tau_{j',n'}+2L} e^{-r\left(s-\tau_{j',n'}-L\right)} v_{\omega^1}\left[s, m, \omega^1, \Omega^-[s]\right] ds + e^{-rL} V_{\omega^1}\left[\Omega^-[\tau_{j',n'} + 2L] \,\middle|\, (x_{j,N_j}, q_{j,N_j}, c_{j,N_j}), f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]\right].$$

On the other hand, if the screening of the compound $\left(x_{j,N_j-1}, q_{j,N_j-1}, c_{j,N_j-1}, \tau_{j,N_j-1}\right)$ is not fruitful, then the expected discounted payoff – discounted to time $\tau_{j',n'} + L$ – obtained by this firm after the patent on the brand ω' has expired is given by

$$(58)\quad A_{29} = V_{\omega'}\left[\Omega^-[\tau_{j',n'} + L] \,\middle|\, (x_{j,N_j}, q_{j,N_j}, c_{j,N_j}), f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]\right].$$

The expected discounted payoff – discounted to the time the patent on the brand ω' expires – earned by the firm which holds the patent on the brand ω' after this patent has expired, given that (i) the firm which holds the patent on the brand ω'' chooses not to carry out any screening when this patent expires, and (ii) the firm which holds the patent on the brand ω' chooses to screen the compound $(x_{j,N_j-1}, q_{j,N_j-1}, c_{j,N_j-1})$ when the patent on the brand ω' expires, is then given by

$$(59)\quad A_{30} = -\gamma_j + \sum_{q_{j,N_j-1}\in Q_{j,N_j-1}[\omega']} A_{28} f_{(\alpha_j[N_j-1],\beta_j[N_j-1])}[q_{j,N_j-1}] + \left(1 - \sum_{q_{j,N_j-1}\in Q_{j,N_j-1}[\omega']} f_{(\alpha_j[N_j-1],\beta_j[N_j-1])}\left[q_{j,N_j-1}\right]\right) A_{29}.$$

The expected discounted payoff – discounted to the time the patent on the brand ω'' expires – earned by the firm which holds the patent on the brand ω' after this patent has expired, given that (i) the firm which holds the patent on the brand ω'' chooses not to carry out any screening when this patent expires, and (ii) the firm which holds the patent on the brand ω' chooses to screen the compound $(x_{j,N_j-1}, q_{j,N_j-1}, c_{j,N_j-1})$ when the patent on the brand ω' expires, is then given by

$$(60)\quad A_{31} = A_{27} + e^{-r(\tau_{j',n'}-\tau_{j'',n''})}\max\{0, A_{30}\}.$$

We are now ready to give the explicit expression for (52) as

$$(61)\quad V_{\omega'}\left[\omega', \omega'', \Omega^{-}[\tau_{j'',n''} + L] \,\middle|\, \left((x_{j,n}, q_{j,n}, c_{j,n})\right)_{n=N_j-1}^{N_j}, f_{(\alpha_j[N_j-1],\beta_j[N_j-1])}[q_{j,N_j-1}]\right]$$

$$= \begin{cases} A_{26}\ if\ the\ firm\ which\ holds\ the\ patent\ on\ the\ brand\ \omega''\ chooses\ to\ \ sreen\ the \\ \qquad penultimate\ compound\ when\ the\ patent\ on\ the\ brand\ \omega''\ expires, \\ \quad A_{31}\ if\ the\ firm\ which\ holds\ the\ patent\ on\ the\ brand\ \omega''\ chooses\ not\ to \\ screen\ the\ penultimate\ compound\ when\ \ the\ patent\ on\ the\ brand\ \omega''\ expires. \end{cases}$$

4.3 Three or More Remaining Unscreened Chemical Compounds

When there remain three unscreened compounds, they might be located in three different chemical libraries or two of them in the same chemical library and the third one in another chemical library. The analysis carried out in Sub-section 3.4.2 can be used as the basis for the backward induction needed to solve the sub-game in which three unscreened compounds remain. Because of the complexity of the model, a simple recurrent relation between the sub-games does not exist.

As we move backward through time to the root of the game tree, we find fewer and fewer brands on the market and less and less information on the potential qualities of the unscreened compounds. The small number of brands on the market at the beginning means less competition on the product market. However, the small number of compounds screened also means less information is available on the potential qualities of the unscreened compounds, and this means more risk is involved in searching for a new drug. According to Toully *et al.* (2002), international pharmaceutical companies now concentrate their R&D efforts not on well-known drugs but on very risky new drugs. This choice might reflect the presumption that the risk involved in carrying out R&D activities in less well-known libraries might be more than compensated for by the market share obtained if the R&D activities are fruitful.

5 Concluding Remarks

Using a dynamic model of optimal patent design and in the presence of information externalities, the evolution of technological progress in the context of a pharmaceutical industry is studied. The preceding literature on the topic works with only one brand, the brand with the highest

quality. As well, the demand is assumed to be completely inelastic. In the conventional models of patent design the role of competitive fringe firms is also discussed implicitly. The model discussed in this research is a continuous in-time dynamic model which provides a rigorous structure for studying the context. It considers several differentiated products, both those whose patents are still in force and those whose patents have already expired, at any point in time. Furthermore the demand for a brand is taken to be a function of income, its price, and the prices of other brands. The interaction of the fringe firm with other patent-holding firms is also explicitly considered under this framework. Unlike the previous literature on the context, the model incorporates both product and process innovation concepts and provides real guidelines to measure the patent breadth. Under this structure, pharmaceutical firms with an active drug discovery program behave strategically in their R&D and in the product markets. Under this structure, three scenarios are discussed: the first scenario refers to the case where all chemical compounds in all chemical libraries are already screened. The second scenario discusses the case where the set of unscreened chemical compounds include only one element. Under this scenario it is shown that the firm which holds the earlier-expiring patent only chooses to screen the last compound, when the patent it holds expires, if the expected discounted payoff net of R&D costs yielded by this action is positive. The expected discounted payoff net of R&D costs obtained by this firm is then decreasing in the cost of screening; increasing in the cumulative quality discovered in the past screenings of the compounds in the chemical library, and decreasing in the number of past screenings carried out in this chemical library. The payoff is also higher if the marginal cost of the drug manufactured from the last compound is lower, and higher if the qualities (marginal costs) of all the other brands – generic drugs as well as the brands whose patents have not expired – are lower (higher). It is also shown that if the firm which holds the earlier-expiring patent chooses not to screen the last compound when the patent it holds expires, then neither will the firm which holds the patent on the rival brand choose to screen the last compound when this patent expires. The expected discounted payoff earned by the rival brand is shown to be decreasing in the cumulative quality discovered in the chemical library, and increasing in the number of past screenings in the chemical library; increasing (decreasing) in the quality (marginal cost) of the brand and decreasing (increasing) in the qualities (marginal costs) of the generic drugs as well as the brand whose patent has not expired. The third scenario refers to the case where the set of unscreened chemical compounds includes two elements. These

elements may be located in two different chemical libraries, or both being located in the same chemical library. Under the first case the analysis suggests that if neither compound is screened by the firm which holds the earlier-expiring patent when it stands alone as the single remaining compound, then it will not be screened either by this firm when it is one of the two remaining compounds. It is also shown that the expected discounted payoff net of R&D costs that the firm which holds the earlier-expiring patent obtains by screening each of the last two compounds is positive, then, every other thing equal, the compound with the lower screening cost should be screened first, the compound from which a new drug with much higher marginal cost is manufactured should not be screened first, and the compound with the potential quality that is stochastically much larger should be screened first. When the elements are both located in the same chemical library the penultimate compound in the chemical library is screened by the firm which holds the earlier-expiring patent, and if the revealed quality of the penultimate compound, is particularly high, then the probability that the quality of the last compound in the chemical library is higher than the quality of the penultimate compound is particularly low, which means the last compound will not be screened.

This work briefly discusses the concepts of patent length and breadth. An interesting extension to this work would be to use the model's formulation to abstract the optimal values for the breadth and length of patent. The model also provides a rigorous structure for analyzing the context under a strategic timing framework. A possible extension to the current work would then be a discussion that offers insights on the impact of strategic timing and the patent race on the subject.

Annex A: The Proof of Proposition 1

PROOF: A rise in the effective marginal cost $\overline{c}_{j\prime,n\prime}$ of the brand $\omega' = (x_{j\prime,n\prime}, q_{j\prime,n\prime}, c_{j\prime,n\prime}, \tau_{j\prime,n\prime})$ shifts both curves $\Phi_{\omega\prime}$ and $\Phi_{\omega\prime\prime}$ upward, inducing a rise in the effective prices of both brands. Because the expenditure on the numéraire good is a constant fraction of $m[t] + \overline{p}_{\omega\prime} + \overline{p}_{\omega\prime\prime} + \overline{c}_{j,n}$, which is higher at the new equilibrium, total expenditures on drugs must be lower under the new equilibrium.

Using the fact that $m[t] + \overline{p}_{\omega'} + \overline{p}_{\omega''}$ is higher under the equilibrium, we can assert that the demand for and a fortiori the total revenues earned by the generic drugs must be higher under the new equilibrium, and this means the market share for generic drugs is higher under the equilibrium.

The rise in $\overline{p}_{\omega''}$, by raising $m_{\omega''}[t] = m[t] + \overline{p}_{\omega'} + \overline{c}_{j,n}$, shifts the inverse demand curve for $\overline{y}_{\omega''}$ upward by the same proportion at each level of demand, and this means an upward shift in the marginal revenue curve associated with this inverse market demand curve. At the new equilibrium, the output, the total revenue, and the profits earned by the brand ω'' are all higher. Also, the market share for the brand ω'' is higher under the new equilibrium.

Using the results just proven that the market share for the brand ω'' and the market share for generic drugs are both higher under the new equilibrium, we can assert that the market share for the brand ω' is lower under the new equilibrium.

Intuitively, we should expect that a higher effective marginal cost of a brand reduces its profitability. However, the technical arguments required to support this intuition are not straightforward. On the one hand, a rise in the effective marginal cost of the brand ω', every other thing equal, reduces the profit earned by this brand. On the other hand, the firm that holds the patent on the rival brand ω'' behaves strategically by raising the per-therapeutic-unit price of its own brand, and this action induces an upward shift in the demand curve for the brand ω', which has a positive impact on the profitability of the brand ω'. Because these two effects are in opposite directions, the net impact of a higher effective marginal cost of the brand ω' on its own profitability cannot be determined unambiguously without some efforts. First, let us rewrite (13), the profit earned by this brand, as follows:

(A.1) $$\left(\overline{p}_{\omega'} - \overline{c}_{j',n'}\right)\left(\kappa_1 \frac{m_{\omega'}[t]}{\overline{p}_{\omega'}} - \kappa_0\right) = \left(1 - \frac{\overline{c}_{j',n'}}{\overline{p}_{\omega'}}\right)\left(\kappa_1 \frac{m_{\omega'}[t]}{\overline{p}_{\omega'}} - \kappa_0\right)\overline{p}_{\omega'}.$$

Note that (A.1) expresses the profit earned by the brand ω' as the product of its total revenue and the factor $\left(1 - \frac{\overline{c}_{j',n'}}{\overline{p}_{\omega'}}\right)$. We have already argued that the total revenue earned by this brand is lower at the new equilibrium. Hence we will succeed in showing that the profit this brand earns

will be lower under the new equilibrium if we can show that the ratio $\frac{\overline{c}_{j',n'}}{\overline{p}_{\omega'}}$ is higher under the new equilibrium. To this end, recall that the equilibrium effective price of the brand ω' is the fixed point of the composite map $\Phi_{\omega'}$; that is,

$$\text{(A.2)} \quad \overline{p}_{\omega'} = \frac{1}{\sqrt{\kappa_0}}\sqrt{\kappa_1}\sqrt{\overline{c}_{j',n'}}\sqrt{m[t] + \overline{c}_{j,n} + \frac{\sqrt{\kappa_1}\sqrt{m[t]+\overline{p}_{\omega'}+\overline{c}_{j,n}}\sqrt{\overline{c}_{j'',n''}}}{\sqrt{\kappa_0}}},$$

Squaring (A.2), and then rearranging the result, we obtain

$$\text{(A.3)} \quad \frac{\overline{p}_{\omega'}}{\overline{c}_{j',n'}} = \frac{1}{\overline{p}_{\omega'}\sqrt{\kappa_0}}\sqrt{\kappa_1}\sqrt{\overline{c}_{j',n'}}\sqrt{m[t] + \overline{c}_{j,n} + \frac{\sqrt{\kappa_1}\sqrt{m[t]+\overline{p}_{\omega'}+\overline{c}_{j,n}}\sqrt{\overline{c}_{j'',n''}}}{\sqrt{\kappa_0}}}.$$

It can be seen immediately that the expression on the right-hand side of (20) is strictly decreasing in $\overline{p}_{\omega'}$. Hence the ratio $\frac{\overline{c}_{j',n'}}{\overline{p}_{\omega'}}$ will be higher under the new equilibrium, as desired. ■

Annex B: The Proof of Proposition 2

PROOF: A rise in the effective marginal cost $\overline{c}_{j,n}$ of the generic drugs shifts both curves $\Phi_{\omega'}$ and $\Phi_{\omega''}$ upward, inducing a rise in the per-therapeutic-unit prices of both brands. Because the expenditure on the numéraire good is a constant fraction of $m[t] + \overline{p}_{\omega'} + \overline{p}_{\omega''} + \overline{c}_{j,n}$, which is higher at the new equilibrium, total expenditures on drugs must be lower under the new equilibrium.

The rise in $\overline{p}_{\omega'}$ and $\overline{c}_{j,n}$ raises $m_{\omega''}[t]$, which shifts the inverse demand curve for $\overline{y}_{\omega''}$ upward by the same proportion at each level of demand, and this means an upward shift in the marginal revenue curve associated with this inverse market demand curve. At the new equilibrium, the output, the total revenue, and the profits earned by the brand ω'' are all higher. Also, because the total expenditures on drugs are lower under the new equilibrium, the market share for the brand ω'' is also higher. The results just established for the brand ω'' also hold for the brand ω'.

At the new equilibrium the lower total expenditures on drugs coupled with the higher expenditure on each of the brands ω' and ω'' imply a lower level of total revenues earned by generic drugs. Also, because the market share for the brand ω' and the market share for the brand ω'' are both higher under the new equilibrium, the market share for generic drugs must be lower under the new equilibrium. ■

Annex C: The Proof of Proposition 3

PROOF: Statement (i) is obvious. To prove (ii), first note that $A_2[q_{j,N_j}]$ is increasing in $q_{j,n}$, and then apply Lemma 1, which asserts that the potential quality of the last compound is stochastically increasing in $\alpha_j[N_j]$ and $\beta_j[N_j]$. Statement (iii) follows immediately from the properties of $A_1[q_{j,N_j}]$. ■

Annex D: The Proof of Lemma 2

PROOF: If the firm which holds the patent on the brand ω'' chooses to screen the last compound when the patent it holds on the brand ω'' expires, then at each age below $\tau_{j',n'} - \tau_{j'',n''}$ during its statutory life, the newly discovered drug has to compete against the brand ω' whose patent has not expired and which is sold above its marginal cost, as well as against the generic drugs in $\Omega^-[\tau_{j'',n''} + L]$. After that and until the end of its statutory life, the newly discovered drug has to compete against all the generic drugs in $\Omega^-[\tau_{j',n'} + L] = \Omega^-[\tau_{j'',n''} + L] \cup \{\omega'\}$.

Now suppose that $A_3 \leq 0$; that is, the firm which holds the patent on the brand ω'' chooses not to screen the last compound. If the rival firm, which holds the patent on the brand ω' chooses to screen the last compound when the patent it holds on the brand ω' expires, and if the screening leads to a patentable drug, then at each age during its statutory life the newly discovered drug has to compete against all the generic drugs in $\Omega^-[\tau_{j',n'} + L] = \Omega^-[\tau_{j'',n''} + L] \cup \{\omega'\}$. Thus, at each age during its statutory life, the patent on the newly discovered drug allows its holder to earn more or the same profit under the scenario that it is discovered by the firm which holds the patent

on the brand ω'' than under the scenario that it is discovered by the firm which holds the patent on the brand ω'. ■

Annex E: The Proof of Proposition 4

PROOF: If the firm which holds the patent on the brand ω'' chooses not to screen the last compound when the patent on the brand ω'' expires, then the discounted payoff for the firm which holds the patent on the brand ω' is given by A_5. If the firm which holds the patent on the brand ω'' chooses to screen the last compound when the patent on the brand ω'' expires, then the discounted payoff for the firm which holds the patent on the brand ω' is still given by A_5 if the screening is not fruitful. On the other hand, if the screening yields a patentable drug, then the discounted payoff for the firm which holds the patent on the brand ω' is given by $A_4[q_{j,N_j}]$, which is lower than A_5, and which is decreasing in the quality of the newly discovered drug. Invoking Lemma 1, we can then assert that the discounted payoff for the firm which holds the patent on the brand ω' is lower when the potential quality of the last compound is stochastically larger. That is, when the cumulative quality discovered in the $jth\ chemical\ library$ is higher and when the size of this chemical library is smaller, the expected discounted payoff obtained by the firm which holds the patent on the brand ω' will be lower. The remaining statements of Proposition 5 can be proved by applying Propositions 1 and 2. ■

Annex F: The Proof of Lemma 3

PROOF: (i) Suppose that the firm which holds the patent on the brand ω'' chooses to screen the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ first.

If the screening is fruitful, then during the time interval $[\tau_{j'',n''}+L, \tau_{j',n'}+L)$ the newly discovered drug competes against the same set of brands – the generic drugs in $\Omega^{-}[\tau_{j'',n''}+L]$ and the brand ω' whose patent is still in force – as if it were discovered under the hypothesis that it stands alone as the last remaining compound. At time $\tau_{j',n'}+L$, when the patent on the brand ω' expires, the firm which holds the patent on this brand will choose not to screen the compound

$(x_{j[\ell\prime],N_{j[\ell\prime]}}, q_{j[\ell\prime],N_{j[\ell\prime]}}, c_{j[\ell\prime],N_{j[\ell\prime]}})$. Indeed, if the firm which holds the patent on the brand ω' chooses to screen the compound $(x_{j[\ell\prime],N_{j[\ell\prime]}}, q_{j[\ell\prime],N_{j[\ell\prime]}}, c_{j[\ell\prime],N_{j[\ell\prime]}})$ when the patent it holds on the brand ω' expires and if the screening is fruitful, then the new drug it discovered will face competition from the drug manufactured from the brand $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ – both before and after the patent on this brand expires – as well as from the generic drugs in $\Omega^{-}[\tau_{j'',n''} + L] \cup \{\omega'\}$. Such an action will yield an expected discounted payoff net of R&D costs that is lower than $A_7^{\ell\prime} \leq 0$, which is clearly not profitable. Thus, if the firm which holds the patent on the brand ω'' chooses to screen the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ first, then the expected discounted payoff net of R&D costs that it obtains will also be given by $A_7^{\ell} \leq 0$. In the same manner, we can show that the firm which holds the patent on the brand ω'' will not choose to screen the compound $(x_{j[\ell\prime],N_{j[\ell\prime]}}, q_{j[\ell\prime],N_{j[\ell\prime]}}, c_{j[\ell\prime],N_{j[\ell\prime]}})$ first when the patent it holds on the brand ω'' expires. We have just shown that when $A_7^{\ell} \leq 0, \ell = 1,2$, the firm which holds the patent on the brand ω'' will shut down its R&D activities and exit the market after this patent has expired.

Invoking Lemma 2, and using the assumption $A_7^{\ell} \leq 0, \ell = 1,2,$ we can assert that the firm which holds the patent on the brand ω' will not choose to screen either compound – if it stands alone as the single remaining compound – when the patent it holds on the brand ω' expires. The argument used for the firm which holds the patent on the brand ω'' can be repeated to assert that the firm which holds the patent on the brand ω' will also shut down its R&D activities and exit the market when the patent it holds on the brand ω' expires.

(ii) Suppose that $A_7^{\ell} > 0, A_7^{\ell\prime} \leq 0$. We have argued that if the firm which holds the patent on the brand ω'' screens the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ first, then the firm which holds the patent on the brand ω' will shut down its R&D activities and exit the market when the latter patent expires. This action yields an expected discounted payoff net of R&D costs $A_7^{\ell} > 0$ for the firm which holds the patent on the brand ω''. Furthermore, because $A_7^{\ell\prime} \leq 0$, when the patent on the new drug manufactured from the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ expires, the firm which holds the patent on the drug manufactured from this compound will not choose to screen

the remaining compound because such an action will not yield a positive expected discounted payoff net of R&D costs. Thus the expected discounted payoff net of R&D costs that the firm which holds the patent on the brand ω'' obtains by screening the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ first will be equal to $A_7^{\ell} > 0$.

If the firm which holds the patent on the brand ω'' chooses to screen the compound $(x_{j[\ell'],N_{j[\ell']}}, q_{j[\ell'],N_{j[\ell']}}, c_{j[\ell'],N_{j[\ell']}})$ first, and if the screening is fruitful, then the newly discovered drug faces competition from same group of competing brands which exist under the scenario that the preceding compound stands alone as the single remaining compound, not as one of the two remaining compounds, plus possibly the potential competition from another new drug that the firm which holds the patent on the brand ω' might develop if the latter firm chooses to screen the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$. Thus, the expected discounted payoff net of R&D costs that is yielded by screening the compound $(x_{j[\ell'],N_{j[\ell']}}, q_{j[\ell'],N_{j[\ell']}}, c_{j[\ell'],N_{j[\ell']}})$ first is not positive, and the firm which holds the patent on the brand ω'' will choose to screen the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ immediately after the patent it holds on the brand ω'' expires. Furthermore, the firm which holds the patent on the brand ω' will not choose to screen the compound $(x_{j[\ell'],N_{j[\ell']}}, q_{j[\ell'],N_{j[\ell']}}, c_{j[\ell'],N_{j[\ell']}})$ when the patent it holds on the brand ω' expires. This firm will shut down its R&D activities and exit the market at time $\tau_{j',n'} + L$, and so will the firm which holds the patent on the brand ω'' once the patent on the drug it develops from the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ expires. ■

Annex G: The Proof of Proposition 5

PROOF: Let us rewrite A_{11}^{ℓ} as follows:

(G.1) $$A_{11}^{\ell} = -\gamma_{j[\ell]} + \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega']} A_{10}^{\ell}[q_{j[\ell],N_{j[\ell]}}] f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]$$

$$+\left(1 - \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega']} f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]\right)\left(\left(A_7^{\ell'} + \gamma_{j[\ell']}\right) - \gamma_{j[\ell']}\right)$$

$$= \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega']} A_{10}^{\ell}[q_{j[\ell],N_{j[\ell]}}] f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]$$

$$+\left(1 - \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega']} f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]\right)\left(A_7^{\ell'} + \gamma_{j[\ell']}\right)$$

$$-\left(\gamma_{j[\ell]}+\left(1-\sum_{q_{j[\ell],N_{j[\ell]}}\in Q_{j[\ell],N_{j[\ell]}}[\omega']} f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]\right)\gamma_{j[\ell\prime]}\right)$$
$$= H_1^{\ell}+H_2^{\ell}-H_3^{\ell}.$$

Note that $A_7^{\ell'}+\gamma_{j[\ell\prime]}$ represents the discounted profits gross of R&D costs earned by the firm which holds the patent on the brand ω'' from the screening of the compound $(x_{j[\ell']},_{N_{j[\ell']}}, q_{j[\ell']},_{N_{j[\ell']}}, c_{j[\ell']},_{N_{j[\ell']}})$ after the unfruitful screening of the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$. Also, recall that

$$A_{10}^{\ell}\left[q_{j[\ell],N_{j[\ell]}}\right]=\int_{\tau_{j'',n''+L}}^{\tau_{j',n'+L}} e^{-r\left(s-\tau_{j'',n''}-L\right)} v_{\omega^{\ell}}\left[s,m,\omega^{\ell},\omega',\Omega^{-}[s]\right]ds$$
$$+e^{-r(\tau_{j\prime,n\prime}-\tau_{j\prime\prime,n\prime\prime})}A_9^{\ell}[q_{j[\ell],N_{j[\ell]}}].$$

Note that the higher is the cost of screening the compound $(x_{j[\ell']},_{N_{j[\ell']}}, q_{j[\ell']},_{N_{j[\ell']}}, c_{j[\ell']},_{N_{j[\ell']}})$, the lower will be the incentive for the firm which holds the patent on the brand ω' to screen this compound in which process might discover a new drug that could compete against the drug discovered by screening the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$. Thus, $A_9^{\ell}[q_{j[\ell],N_{j[\ell]}}]$ will be higher, the higher is the cost of screening the compound $(x_{j[\ell']},_{N_{j[\ell']}}, q_{j[\ell']},_{N_{j[\ell']}}, c_{j[\ell']},_{N_{j[\ell']}})$.

Suppose that $c_{j[\ell],N_{j[\ell]}}=c_{j[\ell'],N_{j[\ell']}}$ and $f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}=f_{(\alpha_{j[\ell\prime]}[N_{j[\ell\prime]}],\beta_{j[\ell\prime]}[N_{j[\ell\prime]}])}$, i.e., the marginal costs of the drugs manufactured from the two remaining compounds are the same, and the probability mass functions that characterize the potential qualities of the two remaining compounds are identical. If $\gamma_{j[\ell]}<\gamma_{j[\ell\prime]}$, then $A_{10}^{\ell}[q_{j[\ell],N_{j[\ell]}}]>A_{10}^{\ell'}[q_{j[\ell\prime],N_{j[\ell\prime]}}]$, which implies $H_1^{\ell}>H_1^{\ell\prime}$, and $A_7^{\ell'}+\gamma_{j[\ell\prime]}=A_7^{\ell}+\gamma_{j[\ell]}$, which implies $H_2^{\ell}=H_2^{\ell\prime}$. Also, if $\gamma_{j[\ell]}<\gamma_{j[\ell\prime]}$, then

$$-H_3^{\ell}+H_3^{\ell\prime}=\left(\gamma_{j[\ell\prime]}-\gamma_{j[\ell]}\right)\sum_{q_{j[\ell],N_{j[\ell]}}\in Q_{j[\ell],N_{j[\ell]}}[\omega']} f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]>0.$$

Hence if $\gamma_{j[\ell]}<\gamma_{j[\ell\prime]}$, then $H_1^{\ell}-H_1^{\ell\prime}-H_3^{\ell}+H_3^{\ell\prime}>0 \Leftrightarrow A_{11}^{\ell}>A_{11}^{\ell\prime}$; that is, every other thing equal, the compound with the lower screening cost should be screened first. ■

Annex H: The Proof of Proposition 6

PROOF: Suppose that $\gamma_{j[\ell]} = \gamma_{j[\ell']}$ and $f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])} = f_{(\alpha_{j[\ell']}[N_{j[\ell']}],\beta_{j[\ell']}[N_{j[\ell']}])}$, i.e., the screening costs and the probability mass functions that characterize the potential qualities of the two remaining compounds are identical. Also, suppose that $c_{j[\ell'],N_{j[\ell']}} \gg c_{j[\ell],N_{j[\ell]}}$, i.e., the marginal cost of the drug manufactured from the compound $(x_{j[\ell'],N_{j[\ell']}}, q_{j[\ell'],N_{j[\ell']}}, c_{j[\ell'],N_{j[\ell']}})$ is much higher than the marginal cost of the drug manufactured from the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$. The differential expected discounted payoff between the action of screening the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ first and the action of screening the compound $(x_{j[\ell'],N_{j[\ell']}}, q_{j[\ell'],N_{j[\ell']}}, c_{j[\ell'],N_{j[\ell']}})$ first is given by

(H.1) $A_{11}^{\ell} - A_{11}^{\ell\prime} = -\gamma_{j[\ell]} + \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega']} A_{10}^{\ell}[q_{j[\ell],N_{j[\ell]}}] f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]$

$$- \left(-\gamma_{j[\ell\prime]} + \sum_{q_{j[\ell\prime],N_{j[\ell\prime]}} \in Q_{j[\ell\prime],N_{j[\ell\prime]}}[\omega']} A_{10}^{\ell\prime}[q_{j[\ell\prime],N_{j[\ell\prime]}}] f_{(\alpha_{j[\ell\prime]}[N_{j[\ell\prime]}],\beta_{j[\ell\prime]}[N_{j[\ell\prime]}])}[q_{j[\ell\prime],N_{j[\ell\prime]}}]\right)$$

$$+ \left(1 - \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega']} f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]\right) A_7^{\ell\prime}$$

$$- \left(1 - \sum_{q_{j[\ell\prime],N_{j[\ell\prime]}} \in Q_{j[\ell\prime],N_{j[\ell\prime]}}[\omega']} f_{(\alpha_{j[\ell\prime]}[N_{j[\ell\prime]}],\beta_{j[\ell\prime]}[N_{j[\ell\prime]}])}[q_{j[\ell\prime],N_{j[\ell\prime]}}]\right) A_7^{\ell}$$

$$= H_4^{\ell} - H_4^{\ell\prime} + H_5^{\ell\prime} - H_5^{\ell};$$

Now if $c_{j[\ell'],N_{j[\ell']}}$ is high enough so that the discounted profits earned from the new drug manufactured from the brand $(x_{j[\ell'],N_{j[\ell']}}, q_{j[\ell'],N_{j[\ell']}}, c_{j[\ell'],N_{j[\ell']}})$ are not sufficient to justify the R&D costs, then $A_7^{\ell\prime} = 0$. When $c_{j[\ell\prime],N_{j[\ell\prime]}}$ is high, but not prohibitive, $A_7^{\ell\prime} > 0$, but not too high. Under this scenario, if the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ is screened first, and if the screening is fruitful, then the drug manufactured from this compound will not face much competition from the drug manufactured from the compound $(x_{j[\ell\prime],N_{j[\ell\prime]}}, q_{j[\ell\prime],N_{j[\ell\prime]}}, c_{j[\ell\prime],N_{j[\ell\prime]}})$. In this case, $H_4^{\ell} \cong A_7^{\ell}$ and $H_4^{\ell\prime} < A_7^{\ell\prime}$, and the differential expected payoff can be approximated by

(H.2) $A_{11}^{\ell} - A_{11}^{\ell\prime} \geq$

$\left(A_7^{\ell} - A_7^{\ell\prime}\right) - \left(1 - \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega\prime]} f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]\right)\left(A_7^{\ell} - A_7^{\ell\prime}\right)$

$= \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega\prime]} f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]\left(A_7^{\ell} - A_7^{\ell\prime}\right) > 0,$

which implies that the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ should be screened first. ■

Annex I: The Proof of Proposition 7

PROOF: The expected discounted payoff differential between screening the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ first and screening the compound $(x_{j[\ell\prime],N_{j[\ell\prime]}}, q_{j[\ell\prime],N_{j[\ell\prime]}}, c_{j[\ell\prime],N_{j[\ell\prime]}})$ first is given by

(I.1) $A_{11}^{\ell} - A_{11}^{\ell\prime} = -\gamma_{j[\ell]} + \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega\prime]} A_{10}^{\ell}[q_{j[\ell],N_{j[\ell]}}] f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]$

$+ \left(1 - \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega\prime]} f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]\right) A_7^{\ell\prime}$

$- \left(-\gamma_{j[\ell\prime]} + \sum_{q_{j[\ell\prime],N_{j[\ell\prime]}} \in Q_{j[\ell\prime],N_{j[\ell\prime]}}[\omega\prime]} A_{10}^{\ell\prime}[q_{j[\ell\prime],N_{j[\ell\prime]}}] f_{(\alpha_{j[\ell\prime]}[N_{j[\ell\prime]}],\beta_{j[\ell\prime]}[N_{j[\ell\prime]}])}[q_{j[\ell\prime],N_{j[\ell\prime]}}]\right) - \left(1 - \sum_{q_{j[\ell\prime],N_{j[\ell\prime]}} \in Q_{j[\ell\prime],N_{j[\ell\prime]}}[\omega\prime]} f_{(\alpha_{j[\ell\prime]}[N_{j[\ell\prime]}],\beta_{j[\ell\prime]}[N_{j[\ell\prime]}])}[q_{j[\ell\prime],N_{j[\ell\prime]}}]\right) A_7^{\ell}.$

If we let

(I.2) $H_6^{\ell} = -\gamma_{j[\ell]} + \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega\prime]} A_{10}^{\ell}[q_{j[\ell],N_{j[\ell]}}] f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}],$

$(\ell = 1,2),$

then we can rewrite (38) as

(I.3) $\frac{A_{11}^{\ell} - A_{11}^{\ell\prime}}{H_6^{\ell}} = 1 + \left(1 - \sum_{q_{j[\ell],N_{j[\ell]}} \in Q_{j[\ell],N_{j[\ell]}}[\omega\prime]} f_{(\alpha_{j[\ell]}[N_{j[\ell]}],\beta_{j[\ell]}[N_{j[\ell]}])}[q_{j[\ell],N_{j[\ell]}}]\right)\frac{A_7^{\ell\prime}}{H_6^{\ell}} - \frac{H_6^{\ell\prime}}{H_6^{\ell}}$

$- \left(1 - \sum_{q_{j[\ell\prime],N_{j[\ell\prime]}} \in Q_{j[\ell\prime],N_{j[\ell\prime]}}[\omega\prime]} f_{(\alpha_{j[\ell\prime]}[N_{j[\ell\prime]}],\beta_{j[\ell\prime]}[N_{j[\ell\prime]}])}[q_{j[\ell\prime],N_{j[\ell\prime]}}]\right)\frac{A_7^{\ell}}{H_6^{\ell}}.$

If the potential quality of the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ is stochastically much larger than the potential quality of the compound $(x_{j[\ell'],N_{j[\ell']}}, q_{j[\ell'],N_{j[\ell']}}, c_{j[\ell'],N_{j[\ell']}})$, then A_7^{ℓ} is much larger than $A_7^{\ell'}$, i.e., $\frac{A_7^{\ell'}}{A_7^{\ell}}$ is small. Furthermore, when the former compound is screened first, there is a greater chance of obtaining a drug of high quality from this action, and thus less chance that it will face competition from a possible new drug that might be discovered by the firm which holds the patent on the brand ω' when this patent expires, and this means $H_6^{\ell} \cong A_7^{\ell}$. Also, $\frac{H_6^{\ell'}}{H_6^{\ell}}$ is small because $H_6^{\ell'} \leq A_7^{\ell'}$.

Thus, when the potential quality of the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ is stochastically much larger that of the compound $(x_{j[\ell'],N_{j[\ell']}}, q_{j[\ell'],N_{j[\ell']}}, c_{j[\ell'],N_{j[\ell']}})$, we have

(I.4) $$\frac{A_{11}^{\ell} - A_{11}^{\ell'}}{H_6^{\ell}} \cong 1 - \left(1 - \sum_{q_{j[\ell\prime],N_{j[\ell\prime]}} \in Q_{j[\ell\prime],N_{j[\ell\prime]}}[\omega']} f_{(\alpha_{j[\ell\prime]}[N_{j[\ell\prime]}],\beta_{j[\ell\prime]}[N_{j[\ell\prime]}])}[q_{j[\ell\prime],N_{j[\ell\prime]}}]\right)$$
$$= \sum_{q_{j[\ell\prime],N_{j[\ell\prime]}} \in Q_{j[\ell\prime],N_{j[\ell\prime]}}[\omega']} f_{(\alpha_{j[\ell\prime]}[N_{j[\ell\prime]}],\beta_{j[\ell\prime]}[N_{j[\ell\prime]}])}[q_{j[\ell\prime],N_{j[\ell\prime]}}] > 0,$$

and this means that the compound $(x_{j[\ell],N_{j[\ell]}}, q_{j[\ell],N_{j[\ell]}}, c_{j[\ell],N_{j[\ell]}})$ should be screened first. ■

Annex J: The Proof of Proposition 8

PROOF: The probability mass function that characterizes the potential quality of the last compound in the $jth\ chemical\ library$, after the quality of the penultimate compound has been revealed, is $f_{(\alpha_j[N_j],\beta_j[N_j])}[q_{j,N_j}]$, where $\alpha_j[N_j] = \alpha_j[N_j - 1] + q_{j,N_j-1}$ and $\beta_j[N_j] = \frac{1}{1+\frac{1}{\beta_j[N_j-1]}}$.

The probability that the quality of the last compound exceeds q_{j,N_j-1} is

(J.1)

$$Prob\left\{q_{j,N_j} > q_{j,N_j-1} \middle| q_{j,N_j-1}\right\} =$$
$$\int_0^{\infty} \left(\sum_{q>q_{j,N_j-1}} e^{-\lambda} \frac{\lambda^q}{q!}\right) g_{\left(\alpha_j[N_j-1]+q_{j,N_j-1},\beta_j[N_j]\right)}[\lambda] d\lambda.$$

With a heavy dose of limiting arguments, we can show that $Prob\left\{q_{j,N_j} > q_{j,N_j-1} \middle| q_{j,N_j-1}\right\} \to 0$ when $q_{j,N_j-1} \to \infty$. However, we eschew these technical arguments and offer a numerical example to illustrate this result. For the simple numerical example, suppose that there are three brands – one generic drug and two leading brands – on the market. The quality of the generic drug is 3. As usual the two leading brands, whose patents have not expired, are denoted by ω'' and ω', respectively, with the patent of the former brand being granted before the patent on the latter. Also, for simplicity suppose that the brand ω'' is obtained from screening the $(N_j - 2)th\ compound$ in the $jth\ chemical\ library$ and that $N_j = 3$. The quality of the brand ω'' is assumed to be 4. As for the brand ω', it is obtained from a different chemical library, and its quality is assumed to be 5. The following table presents the results of the numerical exercise.

Table H.1. The Probability that the Last Compound in a Chemical Library will be Screened as a Function of the Revealed Quality of the Penultimate Compound

q_{j,N_j-1} (the revealed quality of the penultimate compound)	$Prob\left\{q_{j,N_j} > q_{j,N_j-1} \middle| q_{j,N_j-1}\right\}$ (the probability that the drug developed from the last compound meets the leading breadth requirement for a patent)
6	0.263
7	0.223
8	0.191
9	0.163
10	0.140
11	0.121
12	0.104
...	...
20	0.033
21	0.029
22	0.025

As can be seen from the preceding table, the probability that the drug manufactured from the last compound meets the leading breadth requirement for a patent declines steadily as the revealed quality of the penultimate compound rises. When the outcome of the screening of the penultimate compound is particularly fruitful, this probability is so low to render the expected discounted profit yielded by the potential new drug developed from the last compound insufficient to cover its R&D costs. ■

References

Arrow, K. and S. Chang (1982), "Optimal Pricing, Use, and Exploration of Uncertain Resource Stocks," *Journal of Environmental Economics and Management,* 9, 1-10.

Cairns, R. and N.V. Quyen (1998), "Optimal Exploration for and Exploitation of Heterogenous Mineral Deposits," *Journal of Environmental Economics and Management,* 35, 164-189.

Chow, G.C. (1981), *Economic Analysis by Control Methods*, New York: John Wiley & Sons.

Eaton, J. and S. Khortum (2001), "Technology, Trade, and Growth: A Unified Framework," *European Economic Review,* 451, 742-755.

Gilbert, R. and C. Shapiro (1990), "Optimal Patent Length and Breadth," *The Rand Journal of Economics*, 21, 106-112.

Klemperer, P. (1990), "How Broad Should the Scope of Patent be?" *The Rand Journal of Economics*, 21, 113-130.

Mansfield, E. (1961), "Technical Change and the Rate of Imitation," *Econometrica*, 29, 741-766.

---------- (1984), "R&D and Innovation: Some Empirical Findings," in Zvi Griliches, ed., *R&D, Patents and Produ*ctivity, Chicago: University of Chicago Press for the National Bureau of Economic Research.

Nordhaus, W. (1969), *Invention, Growth, and Welfare,* Cambridge, Massachusetts, MIT Press.

---------- (1972), "The Optimal Life of the Patent: Reply," *American Economic Review*, 62, 428-431.

O'Donoghue, T., S. Scotchmer, and J. Thisse (1998), "Patent Breadth, Patent Life, and the Pace of Technological Progress," *Journal of Economics & Management Strategy*, 7(1), 1-32.

Pearlman, R. S. (2009), "Novel Software Tools for Addressing Chemical Diversity," 1995-2009 Network Science Corporation.

Quyen, N. V. (1991), "Exhaustible Resources: A Theory of Exploration," *Review of Economic Studies,* 58, 777-789.

Scotchmer, S. and J. Green (1990), "Novelty and Disclosure in Patent Law," *The Rand Journal of Economics*, 21, 131-146.

Takalo, T. (2001), "On the optimal patent policy," Finnish Economic Papers, Finnish Economic Association, 14(1), 33-40.

Tandon, P. (1982), "Optimal patents with compulsory licensing, "Journal of Political Economy, 90, 470-486.

Toully, V. (2002), *Pharmaceutical Industry: Innovation and Economic Performance: A Study on Behalf of Laboratoires Internationaux de Recherch*, 18 pages