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**PATENTS, PHARMACEUTICAL RAW MATERIALS AND DYNAMIC COMPARATIVE
ADVANTAGES. NOTES CONCERNING THE CASE OF ARGENTINA
AND A RESEARCH AGENDA FOR THE FUTURE ***



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I. Introduction

In a rather long and interesting paper -over 200 pages- three Chilean economists have recently tried to quantify the social cost of strengthening pharmaceutical patent protection in Chile, a developing country which does not presently produce fine chemicals -i.e. pharmaceutical raw materials- but whose three major nationally-owned laboratories currently control 25% of the drug market in value terms and as much as 40% of such market in physical units (F. Coloma et.al.1989).

The fact that Chile does not as yet produce pharmaceutical raw materials allows the authors to concentrate on the consumption side effect of enforcing a stronger patent protection regime, leaving unexplored the production side impact of such policy action. Other Latin American countries -such as, for example, Argentina, Brazil or Mexico, where anywhere between 20% and 40% of their local fine chemicals needs is supplied by nationally-owned firms and where an incipient export trade can presently be observed in this field- would clearly require a more complex research strategy if we are to come up with a dynamic and more adequate judgement as to the future overall impact of granting stronger patent protection in the region.

Given the current North-South debate on the degree of patent protection granted by peripheral countries, and the strong pressure the United States Government is presently putting upon various Latin American countries -consider, for example, the retaliatory action envisaged by the United States authority under Section 301 of the Trade Bill against Argentina or Brazil which have a much weaker patent regime than the one prevailing in the United States- a much weaker regime meaning not only what could or could be not the object of a pharmaceutical patent, i.e. a product or a production process, but also how the Courts would expectedly react in any one specific litigation and where the national jurisprudence actually stands in terms of protecting property rights on new technical knowledge and information -the attempt of coming up with quantitative estimates as to the social cost and benefit of granting stronger patent protection in the pharmaceutical field is much to be welcomed. Quite often both the debate and the formulation of policy prescriptions in this field are carried out under the influence of ideological considerations which foreclose a "rational" examination of the issues hereby involved.

In view of the highly interdisciplinary nature of the questions that belong in the health field in general and in the pharmaceutical territory in particular, the Chilean study -carried out exclusively from an economic viewpoint and under static neoclassical assumptions- has to be understood as a first attempt analytically to deal with the issues, but yet an attempt which could be enriched by taking into consideration aspects which

conventional production and consumption theories do not necessarily take into account. In this respect the Chilean study proceeds along a track opened up by W. Nordhaus some twenty years back (Nordhaus, 1969) and more recently followed by authors such as M. Bailey and S. Peltsman (Peltsman, 1973), which approached the study of the role of patents exclusively as from the standpoint of conventional economic theory 1/.

We shall later on argue that externalities, market imperfections idiosyncratic institutional features of the regulatory environment of any given country etc. as well as dynamic considerations -also not covered by the static welfare maximization model- play a large role indeed in the whole of the health field thus rendering only partially useful results of the sort advanced by the above mentioned studies. It becomes necessary at some point further to enlarge our conceptual perspective bringing in dynamic and institutional considerations which the static model simply leaves somewhat unattended.

After briefly describing some of the major theoretical issues hereby involved -as well as the limitations of received theory for the exploration of many of these topics- and putting the current patent debate within the framework of present day conditions prevailing in Argentina, this paper submits a research proposal specifying major questions which still remain unclear and which certainly demand further research if we are to have a more "rational" approach towards policy formulation in this complex field.

II. A Brief Review of Major Theoretical Issues Involved in the Health Area in General and in the Drug Industry in Particular

Let us begin by identifying some of the central features of the socio-economic environment in which both the production and consumption of health products in general -drugs among them- normally take place. Such exercise will permit us to put into perspective the nature of the assumptions we have to make in order to proceed in this field on the basis of conventional neoclassical principles. Although there are important inter-country differences in the social organization of medicare which at a later stage need to be taken into consideration, most of the aspects we shall now examine are quite ubiquitous throughout.

a) The health care sector is one in which normally the consumer is not the one who chooses the goods and services he consumes, nor is he the one who pays "out of pocket" for most of what he gets.

The therapeutical route followed by any given patient -and therefore his pattern of expenditure- is normally decided by the physician who treats him (who very frequently is also the provider of the medical practice he himself prescribes). Moreover, the bill is normally picked up by a "third party" -an insurance company, the Social Security System, etc. (consider, that two thirds, approximately, of the Argentine population is covered up by the Medical Social Security System, with their contribution to such system being compulsory deducted from their monthly paycheck).

Under such conditions the notion of consumer sovereignty and the welfare maximization theorems used by conventional economics have to be employed with great care. Demand is not necessarily an expression of individual choice under free market and perfect information conditions.

"Common pool" situations and "third party" payment usually call for "excessive entry" (Stiglitz, 1987) whereas the uneven nature of the doctor-patient relationship often allows for over-prescription (IEEE Spectrum, 1989) and overconsumption. Present day Argentina is plagued up with such maladies.

The institutional environment in which the social organization of health care actually takes place -highly different in different societies, as we have previously noticed- is by no means foreign to such situation. The fact that the United States spends somewhere around 2.600 US\$ dollars per person per annum in health care while the United Kingdom manages with around one half of such figure without showing significant differences as far as life expectancy, infant mortality rates and general morbidity charts, illuminates the fact that national institutional idiosyncracies play a large role indeed in this field. In other words, complex issues of social organization of medicare and institutional variables inherent to the particular regulatory regime of any given country can not be easily left aside when we deal with demand of health care goods and services and with drug consumption in particular.

Related to this complex issue we also find questions of imperfect perception of risk (Schwartz, 1987) and externalities which add up further qualifications to the consumer sovereignty approach to health care research and policy making (Katz & Muñoz, 1988).

Turning now to the production side of the market we also find various reasons on account of which perfect competitive equilibrium is far from being the right kind of analytical scenario in which to approach the study of health related issues. Among such reasons we should mention:

b) Market imperfections

Though apparently an unconcentrated industry -no particular firm accounts for more than, say, 8% of total pharmaceutical sales- when we come down to the level of specific therapeutic classes -i.e. antibiotics, tranquilizers, etc.- we notice that quite frequently just two or three firms account for the lion share of the action (Katz, 1974 and 1981). It is also normal that average industrial cost accounts for less than one quarter of total cost -in some cases such as tranquilizers (for example, Valium or Librium), it can be as little as 10% or less- whereas sales and distribution costs take up as much as one quarter or even one third of total costs. Market prices are far off from marginal costs and company behavior should not be expected to be similar to the one received competitive theory makes us a priori to expect.

c) Economies of scale, indivisibilities, etc.

The production of bulk chemicals -i.e. caprolactama, raw penicillin or any other such pharmaceutical "commodity"- seem to be subject to strong economies of scale and physical indivisibilities which render small scale production rather uneconomical. Continuous-flow facilities -increasingly viable today in many chemical and biological fields- constitute a significant technological advance relatively to the previous state of the art -i.e. batch production- but a large market size and a stable demand are sine qua non conditions for its profitable exploitation. Such technological forces are gradually changing market structure and performance -both in domestic markets as well as internationally- forcing a rapid process of business concentration and erecting new barriers to entry. Examples such as E. Lilly's 200 million US\$ dollar human insulin plant opened up in Indiana, and the impact such plant had upon small-batch facilities -such as, for example, the one operated by Lilly in Argentina for the production of bovine insulin, 80% of whose output was exported to the United States- are becoming more and more significant worldwide and deserve careful examination given its long term impact not only upon market structure and performance but also upon comparative advantages of peripheral societies (Bisang et.al, 1988).

Yet another aspect of the scale question comes up in connection to the operation of small-batch fine chemical plants capable of producing just a few tons of specialty chemicals which normally are high priced, recently-discovered and patent-protected. Pharmaceutical intermediaries such as Feldene, Ranitidine, Blufomedil, and dozens of other such valuable active principles belong in this group. This is precisely the area where the patent issue becomes more prominent, as we shall later on see. The simple economics of producing fine chemicals is strongly at variance with standard notions of size and economies of scale inherent in the production of bulk or "commodity" chemicals mentioned above.

Consider as an example the case of Roemmers, the largest nationally-owned pharmaceutical firm in Argentina. It turns out some 70 million US\$ dollars annually worth of final pharmaceutical products. Its fine chemicals plant -Laplex, presently employing some 200 people- produces around 150 tons per year of expensive pharmaceutical raw materials such as those mentioned above, some of them for its own consumption in Roemmers' products, the remaining fraction being sold to other local or even transnational companies.

Conventional screening for new molecules is obviously out of consideration in this case for reasons of scale -consider that discovering and developing a new molecule seems to be costing nowadays just about the same amount of money Roemmers manages to make throughout a whole year. However, not being able to search for new molecules is not really the same thing as being unable efficiently to produce fine chemicals, in particular if such production can be undertaken in small batch conditions and is related to products where markups are high and turnover very quick. To make such arrangement viable Laplex needs to count on a sufficiently large pharmaceutical market -this is where Roemmers plays its major role allowing Laplex needs to cover fixed production costs- and that means operating both locally and in neighboring countries. What we have here is a case of "joint maximization" within the framework of a pharmaceutical "production function" which is far from being a close replica of that prevailing in more mature industrial societies. It is precisely in relation to the viability of production arrangements of this sort where patent protection actually comes foreclosing the expansion of companies such as Roemmers-Laplex on the assumption that by preventing imitation we are in the long end ensuring innovation. The second best nature of the argument comes up quite clearly in this example. Moreover, it is the development of a peripheral society what we are foreclosing under the assumption that such action would eventually enhance profits and innovation of a more developed one. Presumably such action maximizes welfare on a world-wide scale, regardless of its distributive implications.

Economies of scale, externalities, and synergic effects also seem to play a large role in the R&D field. Large multinational companies presently spend somewhere around 300 to 400 million US\$ dollars per annum individually in R&D activities. This comes up to something in the order of 10% to 14% of sales, and sometimes even more. Obviously this constitutes a dramatic barrier to entry to the industry and speaks by itself about the kind of market structure and monopolistic performance likely to obtain in this territory.

d) Externalities

The health field is one in which a large number of externalities underlies the behavior of economic agents, both producers and consumers. Many examples could be given of their

ubiquitous nature and of their importance. Consider the following ones:

- We are frequently told that as a consequence of increased regulation following the 1962 Amendments both the cost and the length of time absorbed by the development of a new active principle have dramatically increased. Truly so, development time went up from 3 to somewhere around 9 years whereas R&D costs boomed up from 5 to, say, 50 million US\$ dollars (and some writers even speak about 100 million dollars or even more). Such argument, however, fails to indicate that as a consequence of at least three more years of clinical research -involving aspects of long term toxicity, immunology, etc.- we now know much more about the potential effects of a new active principle upon the human body than what used to know before. Obviously the relative degree of protection enjoyed by the average consumer has gone up, (which does not really mean that there are not unknown dangers in the administration of any given chemical substance to one particular individual) and this obviously needs to be taken into account even if we can not measure it in any easy way.

- The fact that more research had to be done by pharmaceutical companies in what is called Phases III and IV of the development process necessarily forced them to improve their basic understanding of molecular biology, bio-genetics, etc. "In house" exploratory missions as well as countless R&D contracts with university laboratories have resulted from such a need for further bio-medical knowledge. It seems quite reasonable to assume that recent breakthroughs in bio-medical and bio-chemical sciences -related, for example, to DNA recombinant and other such aspects- have not been entirely independent from what happened some years back in the institutional and regulatory regime in which the United States pharmaceutical industry has been forced to live.

Both previous examples suggest that significant externalities are hereby involved at the macro as well as at the micro level. I just do not know of any specific study that has seriously tried to account for such non-pecuniary effects, but they certainly can not be dismissed lightly.

Summing up: the socio-economic environment in which the consumption, production and search for new drugs takes place is plagued up with market imperfections, economies of scale, externalities, etc. of various sorts. Economic and technological variable, as well as bio-medical, legal, institutional and sociological ones play a large role indeed in the determination of market (and non-market) patterns of behavior. The social organization of health care strongly differs across countries and such differences can scarcely be illuminated if we approach the study of health economics exclusively in terms of received neoclassical production and consumption theories. Such theories provide a first and very useful insight into the order of magnitude

of some of the issues hereby involved but they certainly can not tell us the complete story of what is going on in this field of activity. This is particularly so if we confine ourselves to static welfare maximization models which suppress major dynamic aspects requiring examination.

III. A Research Agenda for Future Studies

On the basis of our previous discussion we now present the contents of a research project aiming at throwing further light upon the questions so far examined.

It is important to begin by recognizing that the overall impact of enforcing stronger patent protection in the pharmaceutical field would be different and more difficult to evaluate in countries in which we already have a domestic industry producing fine chemicals, i.e. pharmaceutical raw materials, than in those others -such as Chile- in which the consumption side effects are probably the only ones that deserve consideration. In our own case the impact upon the production structure as well as upon dynamic comparative advantages and employment can not be dismissed easily. Let us briefly consider why?

About a dozen locally-owned firms presently produce somewhere around one quarter of the country's annual needs for pharmaceutical raw materials. Such industry experienced a dramatic structural change during the late 1970's and early 1980's when the local authorities intended to de-regulate and open up the economy to foreign competition. Four fermentation plants which produced raw penicillin to be used as an intermediary by the antibiotics industry were closed down during the early 1980's. From such point onwards local firms bring in 6APA from abroad -6APA being a "commodity" presently produced under continuous-flow conditions by just five or six large firms in the world- and produce thereafter -through organic synthesis- various types of antibiotics (Groisman & Katz, 1987).

Concomitantly with such developments a number of small-scale multiple-use plants -of the Laplex type, previously mentioned, but of a smaller scale than Laplex- came into being and successfully entered the field of specialty chemicals during the early 1980's. Most of their production is just for selfconsumption in their own product line on the basis of which they act as early imitations and competitors of MNCs subsidiaries operating in the local market. This is certainly a profitable business and clearly one which demands some amount of chemical, bio-chemical, pharmaceutical and pharmacological R&D efforts directed towards the local development of a proprietary small scale process technology as well as to the development and clinical testing of new products.

Perhaps as much as 2% or 3% of sales is accounted for by R&D activities of this sort, but it is obvious that these firms do not carry research in Phase I or II of the new drug development process in the way in which major drug companies do it in developed societies. They certainly do not involve themselves into any kind of effort in the screening for new molecules, though that in itself is not really saying that being an early imitator does not demand R&D activities of your own, or that from a "national interest" standpoint firms of this sort should not be welcomed as would-be competitors. The industrial organization of production strongly differs across countries and we have to be very careful when using standard textbook production models as the basis for our conceptual reasoning and policy formulation.

As mentioned before it is precisely in cases of this sort where the patent protection issue comes up rather strongly. A central feature of the production strategy of fine chemicals producers in peripheral countries is obviously that of being an early imitator of a recently-discovered and expensive new molecule, and being able to develop a small scale proprietary process technology with which to produce such molecule domestically. The violation of property rights will frequently be present in cases of this sort and we can not expect the original owner of the molecule to remain silent.

A number of major questions opens up at this point of our presentation. How would a fine chemicals industry of this sort react to a change in policy regime which would imply stronger patent protection for multinational pharmaceutical companies? Will firms reduce their scale of operation and eventually leave the entire market to foreign companies or, alternatively, will they change their overall business strategy looking, for example, for early licensing agreements with the original owner of the molecule? The tailing off in innovation which is presently affecting large international pharmaceutical houses will somehow help imitators in their bargaining strategy or will it not? The fact that many multinational firms do in fact want to leave the Argentine or Brazilian markets and are increasingly interested in "joint venture" agreements with local firms does make it more likely that negotiations of this sort will actually take place? The recent "joint venture" arrangement between Merck Sharp and Dhome and Sidus suggests that other such cases might come up in the future. Furthermore, how will the local Courts react to a change in legislation? Will the local jurisprudence -traditionally antagonistic concerning patent enforcement- change in the future? And so forth. As we can see, a large number of research questions comes up once we roughly describe the pharmaceutical scenario of developing societies already advanced in the production of fine chemicals. Clearly such questions would require a research program which goes well beyond the measurement of consumer surpluses in a conventional static framework, concentrating exclusively on demand side considerations. The fact that countries such as Argentina,

Brazil or Mexico in the Latin American region or Korea, Israel, Spain or India in Asia and Europe exhibit today a pharmaceutical sector which could in the future attain dynamic comparative advantages and world status clearly indicates that a research program of the sort hereby presented might be very well worth doing.

Note

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