ARE PATENTS, SUPPLEMENTARY PROTECTION CERTIFICATES AND OTHER BARRIERS EFFICIENT FOR PATIENTS AND HEALTH SYSTEMS?

Comments from the AAJM to the Final Report of the consultancy Copenhagen Economics "Study on the economic impact of the Supplementary Protection Certificate and pharmaceutical incentives and rewards in Europe", commissioned by the European Commission (1).

1. Summary

The Report by Copenhagen Economics does not present a clear idea about whether the impact of the Supplementary Protection Certificates (SPC) and the other "incentives" (barriers to competition) are positive or negative for the economy of EU citizens. One is left with the idea that these "incentives" are good for companies, but for society they are like a blanket too small that, if you pull it up, it leaves your feet uncovered and, if you pull it down, it leaves your shoulders uncovered. Thus, the SPC, by extending the monopoly for a few years, gives more profits to companies and, as it is supposed they will use this money for research, generally companies will spend more on research (in the EU as a whole). But, **the Report does not prove that money spent on protection instruments produces more innovation**; it only analyzes if companies spend more on R & D. At the same time, the Report proves that, although all EU countries apply the SPCs and other "incentives", **it does not result in the same availability of medicines in all EU countries**. On the contrary, there are important differences that are due to the wealth and purchasing capacity of each country, that is, to the expectation of profit of the companies. In the same way, the fact that countries apply SPCs and other monopoly instruments **does not improve accessibility**, but rather the opposite, since they increase the prices and expenditure that patients and health systems must make.

Despite this relatively confusing scenario, the report seems to advise that protection times should not be reduced, but perhaps the opposite, since R & D and innovation spending would be increased. The Report recognizes that, if protection were reduced, prices would fall and significant savings would be achieved, but the Report assumes that, as a consequence, companies would not invest in R & D and, thus, the EU would not bring innovation. That is why the authors of the Report believe that an alternative model would not be viable. We do not agree with this opinion. Indeed**, if the barrier of patents, SPCs and other exclusivity instruments were reduced or eliminated, savings would exceed €100 billion per year in the EU-28. That money would be enough for countries to directly invest the €26,59 billion that now they invest indirectly, through pharmaceutical companies, in R & D. In addition, the more than €70 billion remaining, could be invested in other public health policies, in other health and social needs, or could generate savings for the future**. At the same time, "that blanket would cover the feet and shoulders," since it would increase availability and

accessibility in all countries, including those with the lowest income, by marketing the drugs at a "generic price" from the start.

2.Before entering to discuss the Report it is convenient to make some preliminary considerations.

To finance Research on innovative medicines, Public Administrations can use several methods. One is **direct investment** from public budgets, financing research centers, programs, scholarships, grants, awards, etc. Another is **indirectly**, granting a monopoly for the marketing of the medicine to the company that has spent on R & D, prohibiting other companies from selling that medicine for a certain period. By granting that "dominant position", without competition, the companies that have spent on R & D (which we will call originator companies), can put a price higher than what their competitors would put ("generic" price, which covers manufacturing costs and a profit). The over-price is like a "tax" that companies charge to the patient or to the health service. The justification for this tax is that, with that "extra" money that the original company collects, they will be able to recover the costs of R&D.

In the European Union, member countries use the two mechanisms to finance R & D. They directly finance part of the research in medicines (around 30% of total R&D investment), but they also indirectly finance R&D (around 60% of total R&D investment) using different instruments ("protection instruments") to avoid competition for a time, allowing companies to charge an over-price.

The different instruments used to prevent competition are: patents (20 years), supplementary protection certificates (which extend protection up to a maximum of another 5 years), data exclusivity (competing companies can not use for 8 years data from clinical trials of the originator company), market exclusivity (copies of medicines with market exclusivity can not be marketed until after 10 years), orphan drugs (10-year competition ban), pediatric medicines (6 months of extension of the SPCs, and possibility of expanding exclusivity in orphan drugs for children up to 12 years). They are complementary measures that, according to the Report, give an "effective protection against competition" of 13 years from the commercialization of the product. Above that period of "legal" exclusivity, there are other strategies of companies to extend protection and exclusivity, such as the ever-greening of patents, pay for delay, etc., which were studied in detail in the 2009 Commission Report (Pharmaceutical Sector Inquiry).

Comparing the barriers to competition in force in the EU with the measures established in the US, Canada, India, Japan and China, the Report concludes that, on many of the parameters reviewed, **"the incentive framework in the EU is the most attractive one"**. That is, the most beneficial for pharmaceutical companies.

The reason argued by companies to demand various protection instruments, in addition to patents, is that it takes several years since a patent is obtained until the approval to market the drug, and companies do not have as much profit. But, adding

more protection would make sense if we have the certainty that the companies have not yet recovered R & D costs. The issue is that countries are not aware of how much they are paying companies through these "taxes", and what is the difference with what companies are spending on R & D. The figures, as we shall see, are astonishing. There are abusive profits, well above R & D expenditure.

In addition, we know that only a small part of the R & D investment of companies actually produces Innovation, and that most of the Innovation has been made with direct public investment. As Mariana Mazzucato pointed out: *"roughly 75% of so-called new molecular entities with priority rating (the most innovative drugs) trace their existence to NIH funding, while companies spend more on "me too" drugs (slight variations of existing ones."* (2).

3. The Report on the different barriers to competition.

The European Commission commissioned a study on the economic impact of Supplementary Protection Certificates and other incentives and rewards in Europe. The study was carried out by the consultancy Copenhagen Economics, which presented its final report last May.

The objective and content of said contract is as follows:
• Provide an economic evaluation of the incentives and rewards for pharmaceutical innovation in Europe.
• Analyze in particular the effects of SPCs for pharmaceutical uses.
• Examine the evidence on the overall impact on the availability and accessibility of pharmaceutical care for patients and the pressure on EU health systems.
• The evidence and analysis provided by this study will support the formulation of policies in those areas.

The Commission would be studying a readjustment of certain aspects of protection through patents and the supplementary protection certificate (SPC), which could cover the following three elements:
1. the creation of a European SPC
2. an update of the scope of application of patent exemptions for research purposes in the EU, to facilitate the supply of active principles for research purposes throughout the single market.
3. the introduction of an SPC waiver for manufacturing, in such a way that companies established in the EU can produce in the future a generic or biosimilar version of a medicine protected by an SPC during the period of validity of the certificate, if they are made exclusively for export purposes for a market outside the EU where patent protection has expired or never existed.

The Report offers arguments in favor of a unitary SPC (pp. 244 et seq.), pointing out that "fragmentation can distort innovation and incentives". In other words, a unitary

SPC would be more favorable for pharmaceutical companies, would make them earn more money at the expense of taxpayers and patients.

It seems clear that a unitary SPC simplifies the procedures for companies and increases the chances of obtaining a favorable resolution. What the Report does not do, however, is to give solid arguments to justify the maintenance of SPCs and other protection instruments, from the point of view of the interests of patients and taxpayers.

We must not forget that the Commission is requesting this report in a context in which countries are having serious problems in guaranteeing access to medicines due to their high prices. This pressure of pharmaceutical spending erodes health systems. On the other hand, high prices are possible due to the lack of competition that is derived from the monopolies granted by governments to the companies that manufacture the original product (originator companies). And these monopolies are granted to finance the R & D that these companies have carried out.

As the Report states: "What ultimately matters is wheter the company can recoup their initial R & D investment and earn a return on investment ... The period in which this can be done said to be the time running from marketing authorization being granted until the last protection scheme runs out and generics enter the market" (page 94).

In this report, the consultants develop a concept to measure the effective time barrier to competition that the different protection instruments represent for the original brand: the "effective protection period". It is "the time from marketing authorisation until the last form of protection in the form of patents, SPCs, or regulatory incentives and rewards expire, i.e., the effective protection period measures the time a product is on the market and enjoys protection from generic competition via either IP rights or regulatory incentives and rewards". In the study, they estimate that the effective protection period in the EU is 13 years (page 21; page 73).

It is assumed that the Report should make clear what is the economic impact of these measures of protection against competition. It should also document whether these incentives cover the investment in R & D of the companies plus a reasonable profit.

We should answer these questions:
- How much have companies spent on research?
- How much have we paid through the "tax" of patents and other protection instruments?
- What benefit / loss have companies obtained?

The Report does not answer these questions clearly.

What it tries to analyze is the impact of the "effective protection period" on innovation, availability and accessibility.

Regarding the impact on **Innovation**, the Report does not prove that money spent on protection instruments produces more innovation; it only analyzes if companies spend more on R & D (page 96). But it is well known that many R & D expenditures are oriented towards incremental research, "me-too" products, etc. (3, 4).

The conclusion of the Report is that the average protection period in a country does not have a statistically significant effect on the level of R & D expenditure in that country (page 100). What matters to the companies is the level of protection of the countries to which they sell (where they obtain those over-prices supposedly destined to pay the R & D), as well as the wealth of the other EU countries with which a given country trades the most in pharmaceuticals.

Companies that sell their products in countries that have more protection (more time without competition, with higher prices to recover R & D expenses) tend to spend more on R & D. As the laboratories that are in European countries sell, in part, to European countries where there is protection against competition, they invest more in R & D than if there were no such protection. This conclusion was expected. That is, if we pay more money through the patent protection tax and other instruments that extend that protection delaying competition, and we pay it for companies to do research, it is logical that they spend more on research. The question is whether they spend everything we pay them with the over-price to do research, how they spend it and how much profit they get. We'll see later.

It should be noted that, when assessing the impact on Innovation, the Report only analyzes whether companies spend more or less on research, but does not analyze whether the research expenses of the companies are oriented to health needs, are innovative or incremental, are duplications of other investigations, or if they include promotional expenses (payment to doctors for phase IV clinical trials) as if they were research expenses, etc., etc.

Regarding the **availability** of medicines in the different EU countries, the report concludes that it is not favored by these instruments of protection against competition. That is to say, there is no evidence that, if the protection time is increased (with SPCs or other instruments), companies launch their products in different European countries at the same time (page 133). On the contrary, the data show that they are launched at different times or not launched at all, depending on other factors, especially the country wealth, its purchasing power. The Report estimates that, in the 20 years since the first international launch of a new molecule, laboratories have only released that molecule (made available) in just over half of the EU Member States (page 125). The Report notes that **there are large differences between EU countries in terms of the delay in which a molecule is available**. The two variables that, according to the Report, influence in which the medicine is launched before in a country are the wealth of that country (GDP) and the size of the population, but not the instruments of protection. "The implication of the result is that some countries receive new medicinal products much faster than others, while some

medicinal products never become available outside a range of more affluent countries" (p.128).

Regarding the impact on the **accessibility** of medicines in the different countries of the EU, the Report notes that it is negatively affected, since the entry of competition is delayed, and therefore there is no price decrease. As the originator companies put higher prices, the cost that the countries support is higher. Is the investment of companies in innovation covered by this increase in expenditure? Or, is it smaller or bigger? This is a key point. However, the Report recognizes that: "The problem is the asymmetric information possessed by the parties. **Generally, the authorities will not be able to check whether the pharmaceutical companies have recouped their R&D investment and obtained a return on investment sufficient to reinvest in developing new innovative medicinal products in the future** "(page 29). This is very serious, since this was the justification for patents and other exclusivity instruments. It means that **countries give money (over-prices) to pharmaceutical companies "blindly**". The Report also recognizes that in the scenario of maximizing the benefits applied by the industry, these incentives do not lower prices and only serve to increase the profits of pharmaceutical companies at the expense of the payers.

4. What is the economic impact of patents and other protection instruments in health systems? Do patents and SPCs benefit patients and Health Systems, or do they benefit only companies?

To calculate the excess of expenditure incurred by patients and health services when financing research through "protection instruments", the Report makes a calculation comparing the price difference of the generic drug in the first months of its entry in the market with the price of the originator medicine at the time the generic enters (or a few months before). The report finds that the prices of generics in the first months since the loss of exclusivity are around 50% of the prices that the brand had at that time. And it makes an estimate on what it would mean to replace 10% of the volume of brand sales with generics. Assuming that the total cost in medicines of the EU, was $ 247 billion (OCDE, 2015) and 76% of the sales were of branded medicines, the obtained savings would be $ 12.4 billion. But, it is important to note that, if 100% of brand name drugs were sold at generic price, the savings would be $ 93.93 billion (ie € 79.77 billion) (see Graph in page 161).

However, to assess the impact of protection instruments considering that the average of the prices of generics with respect to the corresponding brand-name drugs is 50% lower, is an important bias. Savings for taxpayers (or current over-spending) should be estimated by measuring what original medicines cost over 13 years of protection against competition, and not with the price at the time of losing exclusivity, which it has generally gone down to prepare to compete with generics. Likewise, the prices of generics should be considered over several years, when there is more competition with other generics, and not the price of the first months. For example, in the work of Berndt and Aitken (2010), quoted in the Report, they saw that the prices of generic

drugs (between 2005 and 2009) fell in the US from 100 to 68 in the first 12 months following the entry of the generic, and went down to 27% of the initial price at 24 months. Also, an analysis of the FDA cited in the report also shows that generic prices would be 25% of brand prices. With this difference in price, and a substitution of all branded drugs for generic, the expense would be as follows: generic drugs, $ 59.28 billion; brand-name drugs at a generic price of $ 46.93 billion; total expense at the price of generics, $ 106.21 billion; the savings for patients and health systems would be $ 140.79 billion (page 175), about € 118.98 billion. Much more than all the R & D expenditure carried out by companies.

Indeed, pharmaceutical companies have declared an expenditure of €26,59 billion (data from EFPIA for 2016). The difference with the € 118.98 billion that patients and taxpayers pay for companies to do R & D through protection instruments amounts to € 92.39 billion. A lot of money! Exaggerated benefits for companies and a very high cost for citizens of the EU.

This approach, to calculate how much we would pay for all medicines if they had generic price, and what margin we would have left to pay all the R & D, was already raised by Dean Baker when he wondered if it were possilbe another way to finance the development of medicines. Using an estimate for the US, the conclusions were the same: yes, it is possible, and significant savings would also be obtained (5).

With these data it would seem clear that the barrier of protection against competition can and should be reduced, eliminating SPCs and other exclusivity instruments. But the Report does not pronounce in this sense, but rather on the contrary. Let's see why.

5. To finance R & D directly or indirectly through the tax on patents and other instruments of protection against competition?

The report warns that, if the protection times against competition are reduced (and, therefore, the income paid by patients and health services for R & D through overpricing), "It may be that originator companies would change their R & D effort" (page 159). And they conclude that pharmaceutical research spending would fall. It may be that development times will increase and that the time to get to market would be delayed. "In effect, this would slow the pace of innovation within the pharmaceutical industry,"... “which would be to the disadvantage of patients”.

The authors of the Report add that the scenario of maximum savings, where all drugs are sold at the price of generic, is "inconceivable" and "unrealistic" because companies would not invest in R & D and the EU would not contribute to the discovery of new medicines, but would take advantage of the expenses of other countries that would continue to pay over-prices. This would create an international uproar (page 162). But what the report does not say is that a) the EU countries are already making a significant direct investment in medicines R & D (more than 30% ot total R&D

expenditure), and b) the EU countries, in the new scenario, could continue to devote € 26,59 billion to R & D, or even more, with direct investment.
Obviously, if the EU and the Member States decided to reduce protection times and, consequently, the benefits of pharmaceutical companies, this lower expenditure (€118.98 billion) should be reinvested in R & D and other health policies. As we have seen above, if the protection were totally eliminated, the R & D expenditure could be maintained (€26.59 billion) and also save €92,29 billion. And, in this way, the pace of innovation would be maintained, or increased, and there would still be a very important remnant. **The key innovation would be that Government Institutes and independent Academic Centers should complete research and development of medicines until obtaining approval for commercialization.**

The economic impact of the new model would be significant and positive for patients and health systems. The results of the research would be open and would benefit all countries, as would access to medicines at the price of generics.

It is worth mentioning another fact that the report does not specify either, being fundamental to justify the patent model: pharmaceutical companies in the EU declare pre-tax profits that are more than double that of other companies in the industrial sector. In addition, they allocate a large part of their income to marketing (double the percentage of sales over other sectors) and other large amounts to repurchase shares, mergers, purchase of companies, etc.

6. What then is the economic impact of SPCs and other exclusivity measures?

Now we can answer the question about the economic impact of the protection measures we were doing at the beginning:

- How much have companies spent on research in the EU-28 ?: €26.59 billion
- How much have we spent with the "tax" on patents and other instruments of protection in the EU-28 ?: € 118.98 billion
-What benefit have the companies obtained ?: more than double the rest of the sectors.

We could conclude that the economic impact for taxpayers, patients and health services of the current model of financing R & D with measures to protect exclusivity is negative, while for companies it is very positive.

But, in addition, **reducing or eliminating protection against competition in medicines would improve availability and access**. In effect, since there is no patent (the patent would be owned by the people, since R & D would have been paid with public budget) the price is generic in all countries, and manufacturers are interested in launching their products in all markets, because people can buy them. On the other hand, since it is a generic price, public health systems can finance these medicines, which increases accessibility for all the population.

To these advantages are added other important ones. Research no longer has commercial pressure, so priorities are marked in relation to health needs. For example, you can invest in public health research (prevention and promotion), primary care, nursing, etc. The investigation has no bias, since the manufacturer does not pay for the investigation. The research focuses on innovations, and not on incremental research (copycat research, in which 2/3 of resources are currently spent). The research does not need to be repeated by different originator companies, since it is open and the results are public. The training of professionals is financed by the savings of the new model, which reduces the pressure on the prescribers, and reduces the unnecessary prescription and adverse effects of medicines, whose cost in lives and expenses is very high.

These would be some of the positive impacts of progressively reducing and replacing patent protection and other exclusivity instruments, through direct financing of R & D.

Of course **it is not easy to change the model due to the enormous pressures of the companies**, and the enormous volume of resources that they allocate to marketing and lobbying with the resources that society gives them through the over-prices. But it is possible to be aware that it is convenient for the citizens of the EU to change this model. And it is possible that some governments initiate actions for change and make proposals in this sense within the EU. For example, a progressive discount on sales volume aimed at creating national and EU Funds for research managed by countries (not by companies).

A new model, reducing or eliminating drug patents and other exclusivity instruments, is realistic, efficient, and consistent with the consideration of medicines as a right and not as a business. Only with a new model for financing R&D of medicines will it be possible to guarantee the right to health of all people in the EU and in all countries of the planet.

REFERENCES

1).https://www.copenhageneconomics.com/dyn/resources/Publication/publicationPDF/5/445/1527517171/copenhagen-economics-2018-study-on-the-economic-impact-of-spcs-pharmaceutical-incentives-and- rewards-in-europe.pdf

2). Mazzucato, Mariana. How taxpayers Prop Up Big Pharma, and how to cap that. Los Angeles Times. October 27th, 2015. http://www.latimes.com/opinion/op-ed/la-oe-1027-mazzucato-big-pharma-prices-20151027- story.html

3). Rev Prescrire. New drugs, new indications in 2015: Little progress, and threats to access to quality healthcare for all. February 2016; 36 (388): 133-137

4). Prasad V, McCabe Ch, Mailankody S 2018. Low value approvals and high prices might incentivize ineffective drug development. Nature Reviews Clinical Oncology. 15 May 2018.

5). http://cepr.net/documents/publications/intellectual_property_2005_10.pdf