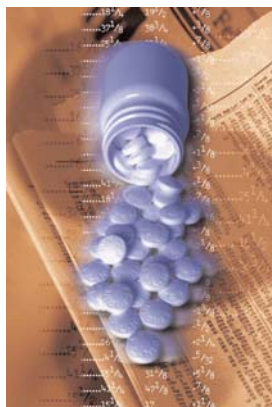


Hidden defects in the authorisation procedure of placing drugs on the market

The authorisation body for the introduction of drugs on the market of the French Agency for the medical safety of health products (AFSSAPS) announced in September 2005 the banning of Solutricine, Lysopaïne and 10 other products aiming at reinforcing immunity, because rare adverse effects of an allergic or a cutaneous nature would have appeared. The regulator poses as a guard to public health because beyond the vigilance which it exerts with respect to products already on the market, it requires pharmaceutical laboratories to perform a series of safety and effectiveness tests for every new product, before authorizing them to be put on the market. It could thus offer an essential protection against otherwise dangerous products to which patients would be exposed if such an obligation did not exist.

However, ensuring the safety and the effectiveness of the drugs is necessarily costly. From the point of view of patients, an arbitrage between these concerns and that of obtaining the products is always necessary. But the AFSSAPS tends to support an excess of precaution to the detriment of all those who are deprived of care on this basis. Moreover, it cannot respond to different requirements from a multitude of people. It is the bureaucratic and monopolistic character of decisions within the agency which is in question. Consequently, the introduction of competition into the drugs certification process should be considered *vis-a-vis* the prospect of a *status quo*.



Obviously, the other side of the coin story becomes visible: patients would be condemned to seeing their health deteriorate due to lack of care. Faced with this dilemma, the regulator weighs up the benefits and the expected risks of a product in taking a decision².

However, another consideration must be taken into account. When drugs are finally authorised, it means that the regulation authority decides to regard them as sufficiently safe and effective.

That means ipso facto that these drugs could not legally benefit patients throughout the duration of the authorisation procedure. Thus, it would be advisable not to forget the suffering and the deaths that are not avoided because of the delays imposed by the procedure.

The neglected costs of the procedure

From the point of view of patients, the problem of placing health products on the market is not reduced to a simple reduction of its risks. It would be illusory to hope to settle it by entrusting an extraordinary power to a regulator who would carry out increasingly drastic controls. Indeed, if the risks related to the side effects of drugs are the only ones to take into account, why not simply ban these products, rather than test them prior to a possible authorisation? One would thus be certain of keeping patients safe from these side effects!¹

Moreover, the generally neglected costs of such a procedure are not reduced to these delays. As it must mobilise resources which could have been used differently by pharmaceutical companies, the costs of research and development of products are higher. Consequently, the profitability of innovations is decreased and certain products are not subjected to the procedure, because they are quite simply not developed. The drugs being used for the treatment of certain rare diseases are among the first not to appear on the market because of this.

¹ The precautionary principle establishes that "where threats of serious and irreversible damage exist, the lack of scientific certainty should not constitute a reason to postpone measures aiming at preventing environmental degradation". Consequently, such a ban would be a literal application of the precautionary principle to the introduction of drugs on the market. On the dangers of the precautionary principle, cf. Precaution with the Precautionary Principle, IEM, March 2005

² Cf. Jean Marimbert's speech, General Director of the AFSSAPS, to the conference "Risqué, opinion publique", Université de Paris Dauphine, 23 March 2006.

There is no perfect solution. The safety and effectiveness of drugs cannot be free. To advance or delay their placement on the market has advantages and disadvantages. Thus, it can be decisive, so that a patient and his doctor agree on a treatment, to know that tests have not revealed significant danger. Rather than use the treatment immediately, if it is available, they can judge that the inconvenience of waiting a certain time is well worth the information produced thanks to tests. But whereas information accumulates with waiting, they can consider - more or less quickly according to their aversion to risks - that enough is known about the product to make use of it³.

Depending on pathologies, according to the judgement of each one, the "right moment" to buy a drug, the good arbitrage between the assurance of a certain safety and the disadvantage of not undergoing care, can be different. It is on the other hand certain that no solution claiming to offer maximum safety and effectiveness without holding account of the implied delays can be regarded as ideal from the point of view of the people requesting care, precisely because it ignores their priorities. Thus, estimates of the benefit/risk ratio used by the regulation authorities to judge the advisability of authorising a drug should include another dimension, that of the costs of waiting. Without it, the aspirations of the people firstly concerned, the patients, would be neglected.

Sources of regulation authorities' inefficiency

The authorisation procedure for introducing drugs on the market is done badly in more than one respect with the declared objective of working for citizens' health. First of all, the regulation authority tends to impose excessive delays because it is encouraged to neglect the costs of waiting compared to effectiveness and safety considerations. To identify the source of this bias, it should be understood that agency decision makers are men like any others. They prefer to earn money, to gain prestige, reputation, etc, rather than to lose them, or to even lose their job. One must thus expect that the objective of serving their fellow citizens is pursued insofar as it is in harmony with the objective of improving their own lot, neither more nor less than in other sectors of activity.

“It would be advisable not to forget the suffering and the deaths that are not avoided because of the delays imposed by the procedure.”

“By supporting safety and effectiveness without regard to the costs of waiting, the agency tends to block the sale of reasonably satisfactory products from the point of view of the patients.”

In this context, to serve their fellow citizens means avoiding two types of errors related to the introduction of medical products on the market. Either a drug is accepted "too early" in terms of the best patient arbitration between safety, effectiveness and availability, or it arrives too late. The objective of improving their own lot consists for people working at the regulation agency of obtaining the highest possible budgets on behalf of politicians. The amount of this budget thus depends on the reputation of the agency within public opinion. Consequently, it becomes fundamental, for the agency wishing to preserve or increase its budget, to avoid any media scandal related to the introduction of a drug on to the market. From this point of view, the agency may find it beneficial to be concerned with the safety of products. But what about costs related to marketing delays?

When a drug reduces a death rate from 40 to 30%, the 10% people who would otherwise have died remain unidentified. Nothing spectacular there. During the authorisation procedure, mortality due to its absence on the market does not cause scandals because the victims of the delay and their family, are not generally aware of the existence of the products and do not know what hit them. They just know that nothing can be done for them. The decisions of the agency will then be biased against the introduction of new products, the losers of the procedure being condemned to suffer in silence. By supporting safety and effectiveness without regard to the costs of waiting, the agency tends to block the sale of reasonably satisfactory products from the point of view of the patients, either by lengthening the time for placing them on the market, or by prohibiting them. The excess of protection does patients a disservice by paralysing the introduction on the market of treatments⁴.

In addition, the procedure is of a "one size fits all" type. One allows a product to be sold to everybody or no one. However, it should be clear that even from a purely physiological point of view, individuals are different. A very risky product for one person is not so for another and the effectiveness of a drug is different depending on patients. Moreover, these have different priorities. Depending on the aversion to risk of each one, the right moment to introduce it on the market will be different. Thus, whatever the compromise decided

³ Cf. Robert Higgs, *Banning a Risky Product Cannot Improve Any Consumer's Welfare (Properly Understood), with Applications to FDA Testing Requirements*, Review of Austrian Economics, Vol. 7, n° 2.

⁴ Cf. Robert W. Hansen, "FDA Regulation of the Pharmaceutical Industry", in Robert Higgs, ed., *Hazardous to our Health*, The Independent Institute, 1995.

by the regulation authority between the accumulation of knowledge and product availability, certain patients will be harmed.

Even in the absence of a bias against the introduction of new products, the regulator would in any event find it hard to discover means of adjusting its decisions to the various preferences of patients. The signals revealing a bad choice of agency are in effect limited to the large media scandals. That hardly constitutes a criterion to judge the adequacy of its decisions with the best compromises between effectiveness, product safety, and waiting costs, for various categories of people characterised by different physiological attributes and diverse and changing preferences as regards aversion to risk. Under these conditions, the determination of the "right moment" to authorise a drug onto the market is strongly marked by a good measure of arbitraire.

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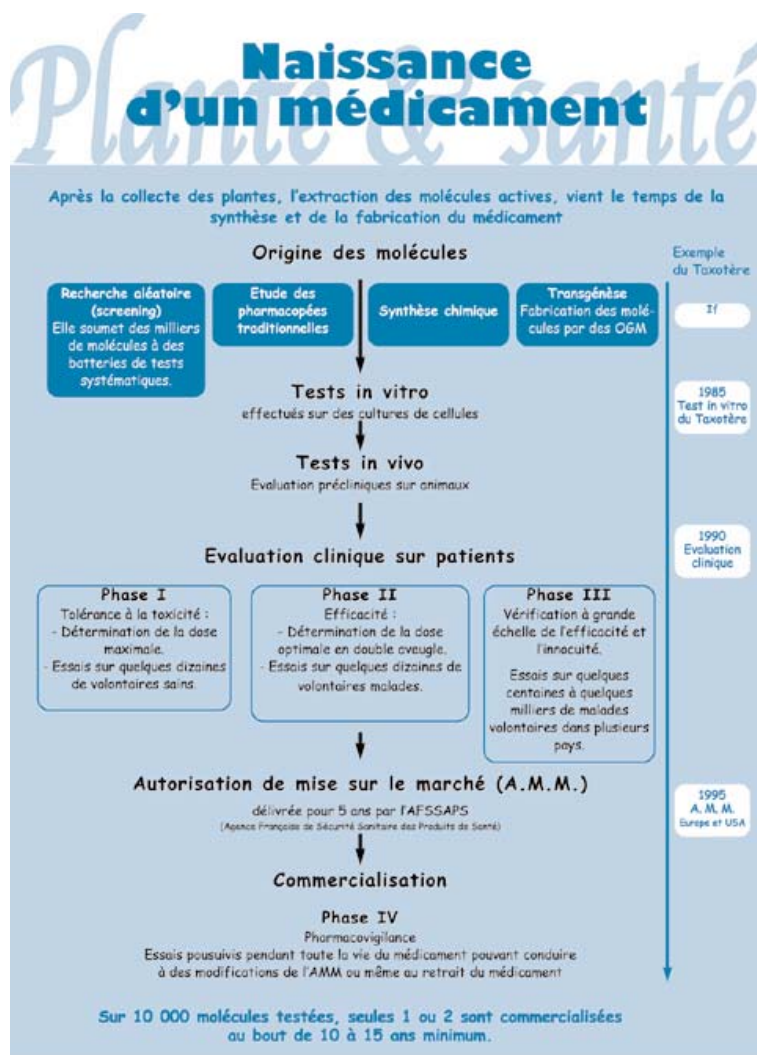
Competition in the certification of products

If there is no miracle solution to guide the trade-off between safety, effectiveness and the delay in placing drugs on the market, patients' interest certainly requires exploring solutions making it possible to approach the best possible compromises. An approach consists in observing what happens in other industries and in trying to draw some lessons from them. After all, the health products regulation agency exerts a certification job and many other products are the object of a certification of their conformities to standards of a voluntary nature as to governmental regulations, without a legal monopoly of certification existing.

In fact, this practice is so widespread that one can very easily find its trace in one's everyday life: computers' power supply, for example. There are strong chances of finding a "UL" logo there. *Underwriter Laboratories* is a company set up in 1894 in the United States. At the time, electric connections posed serious safety problems. Many fatal fires were linked to problems of electric safety in large cities. It was to meet a need to test and guarantee the safety of installations that UL was created. Since then, this company specialised in the electric and electronic fields widened its activities by certifying the competences of aircraft pilots, by creating standards for building materials, etc. Today, it ensures the quality of thousands of products in 97 countries⁵.

How does that function and which lessons can one draw on for the introduction of drugs on the market? UL thrives insofar as the building material or computer makers do not turn to competitors. To find its customers, the certification company had to develop and preserve a reputation of independence and effectiveness guaranteeing the value of its label to its customers and finally consumers. Indeed, the reason why customers are ready to support the added spending of this certification and to yield to the requirements of UL is a hope of seeing the value of their products increasing with the obtention of the label. They would have an interest in turning to other companies if UL had the reputation of allowing itself to be corrupted. The certification companies and their customers are strongly encouraged to play the game because infringing the rules would amount to renouncing their profits and to giving their competitors a gift.

This compass of losses and profits within a competitive framework also obliges the certification



⁵ Cf. The website of Underwriter Laboratories, Inc.

specialists to adopt standards of safety, product effectiveness and waiting costs according to the priorities of the end-buyers. If the initial tests delay five years the introduction of the product on the market whereas less complete tests would have been sufficient, the profits will go to those - certification companies and owners of the certified product - which will have best fulfilled the consumers requirements by putting their product on sale earlier. Lastly, insofar as the consumers, who ultimately determine the financial results of all these actors, do not all have the same priorities, certification companies may find it beneficial to develop various adapted labels.



Incentives allowing certification companies to concern themselves with the best compromises between safety, effectiveness, and timings of market introduction, are lacking in the medical regulation authority. One could thus consider allowing competition between the State agency and private certification agencies. Under these conditions, pharmaceutical laboratories would turn to the organisation of their choice according to the reputation that the label would give them among doctors and patients.

“To avoid as much as possible the excess of precaution as a too weak effort on the safety and effectiveness of the products, it would be advisable not to neglect the route of competition of the regulation agency with private certification organisations.”

Compromises between safety, effectiveness and delays would get closer to the requirements of doctors and patients: insofar as a product would arrive too early on the market, without sufficient guarantees of safety and effectiveness for patients and their doctors, the label would be devalued in their eyes and the agency would offer an opportunity for profit to competitors presenting a label representing a better compromise. Insofar as it would arrive too late, the product would also be sanctioned by the expenditure report of the patients towards products offering a better compromise. And the incentive to continue the tests after placement on the market would play so as to gain the confidence of doctors who are not ready to prescribe them so early, while meeting the needs for different safety-effectiveness-availability trades-off.

Conclusion

The introduction of drugs on the market inevitably presents risks, but as safety and effectiveness cannot be free, it is necessary to apprehend all dimensions of decisive choices for the wellbeing of all. Trades-off between the search for safety, the effectiveness of products and their more-or-less rapid provision to the public, must in any event take place. The current procedure of authorising the introduction of drugs on the market tends to neglect the disadvantages of a late placement on the market without regard to patients' priorities, because its monopolistic position encourages it. A reflection on the improvement of the system must concentrate on the means of adjusting the decisions closer to the trades-off wished for by patients and their doctors between safety, effectiveness and availability. To avoid as much as possible the excess of precaution as a too weak effort on the safety and effectiveness of the products, it would be advisable not to neglect the route of competition of the regulation agency with private certification organisations.

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