

## **Research and development of orphan drugs: At last a European regulation**

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### **1. Introduction**

The European Parliament adopted in second reading, at its plenary session, last December in Strasbourg, the draft Council Regulation concerning orphan medicines.

Aiming at the rare diseases, and therefore to a very limited number of patients, these medicines do unfortunately not constitute any profitable market. The pharmaceutical industry is therefore not much inclined to devote research and development budgets to them.

The French Presidency of the Council in 1995 is at the root of this project. France is the only Member State to have created, in the same year, a ministerial task force on orphan medicines. The remarkable work completed by the latter allowed the drafting of a text proposed by the European Commission in 1998.

### **2. The reasons for this initiative are numerous**

The most important one is of an ethical nature. Today, in our developed societies, it is not tolerable to exclude certain categories of patients from scientific progress on the pretext that the illness from which they suffer is rare. About 5 000 illnesses of this type are currently indexed. They are all extremely serious, disabling heavily and mortal in the more or less distant future. They touch almost 8% of the European population, namely, 25 to 30 million patients. The cause is noble and the challenge certainly worth the effort.

But, pharmaceutical research and development are very expensive and random. Before meeting a success, laboratories pass through numerous failures. Concerning the rare illnesses, research is more difficult and hazardous as the low number of patients make the tests and the experimenting very delicate to be carried out. Without specific motivation, industrialists do not launch this type of research, for which they have no commercial interest. Orphan medicines already present on the market were often discovered by chance and are useful for other medical current indications, making real profits possible.

The second reason is of an economic nature. Europe is very late compared with Japan, and with the United States which adopted a law “orphan drug Act” in 1983. Thus, in the absence of an adapted legislative framework in Europe, some large laboratories, in particular the British multinationals established on American soil, registered orphan medicines in Washington. Thanks to these legislative tools, 900 medicines could be designated and almost 190 have already been marketed in the United States and 45 in Japan.

Europe created in 1995 a Community marketing authorisation procedure of medicines. It concerns a population of more than 370 million individuals and has, with more than 2 000 pharmaceutical firms and 500 biotechnological firms, a research potential at least equivalent to that of the United States. It could not remain behind longer.

Lastly, the third reason is scientific. Research and development of this type of medicine is primordial. The example of the AZT is very significant. In 1985, the Wellcome laboratories registered in Washington, as an orphan medicine, this product destined for HIV patients. At the time, the small number of patients made of AIDS a rare illness. Without this specific statute recognised by the “orphan drugs Act”, it is very likely that the Wellcome financiers would not have taken the risk of launching such a research and development programme. Today, this treatment and others are making it possible to look after and relieve thousands of patients.

### **3. What are the aims of this regulation?**

It aims to support development and search for medicines, intended to detect, to prevent or treat the rare illnesses (i.e. the prevalence of which is of 5 persons for 10 000 on the territory of the European Union), or the illnesses putting life in danger, the very invalidating illnesses, the serious and chronic illnesses and the diseases which marketing is considered unprofitable.

“Orphan medicines” designation is valid for the “product/indication” couple. Industrialists have to show that the medicine represents progress, either because it is more satisfactory than the already existing methods, or because it gets a considerable profit for the patients suffering from these affections.

The European text is widely inspired by the American experiment which constitutes to date a genuine success. It envisages incentives, intended to encourage the industrialists. The principal lever is the granting of commercial exclusiveness in the market for 10 year, granted to the “product/indication” couple. That represents for the company a commercial outlet guarantee on a limited market. The second lever is aid for the development of the clinical protocols which will be brought by the European Agency for the Evaluation of Medicinal Products. This involves helping the industrialists to assemble their development file. The principal difficulty is connected with the clinical trials and with experimenting, with the fact that patients are not very numerous and disseminated throughout the Community territory.

If one trusts the American experiment, innovative, small and medium-sized enterprises will make use of these incentives more than the large pharmaceutical laboratories. The small structures specialised in biotechnologies in particular will be concerned since the immense majority of the rare illnesses are of genetic origin.

After its joint adoption by the European Parliament and by the Council of Ministers, this new regulation applies directly in all the Member States. This involves immense progress, because the innovative industrial solutions will allow to answer a genuine public health problem.