Original, generic medicines and copy

the questioning of the precaution principle

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Empirism. Pragmatism

- Creation of an autonomous status

Generic medicines in Europe

March 31st, 2004, generic medicines acquire a real legal status in the directive 2004 / 27 / EC

- Nevertheless,
  - should the patient be the center of the reflection,
- the " reality of the facts shows that the development of the generic medicines and their usage derive from a certain economic opportunism "

  (Cendrine Barthelmé)

Generic medicines in Europe

March 31st, 2004, generic medicines acquire a real legal status in the directive 2004 / 27 / EC

- The Incentives in favour of this new type of medicines,

- are mainly of *pecuniary order* :
  - ***subsidies*** to the doctors
  - ***premiums*** for the replacement to the pharmacists,
  - ***return on investment for the industrialists***

Directive 2004/27/EC and Marketing authorisation (MA)

- Sets up a procedure of **abbreviated, specific MA for generic medicines**

- **" A generic medicine of the reference medicine authorized by the community can be authorized by the proper authorities of Member states according to the directives 2001 / 83 / Ec and 2001 / 82 / Ec in the following conditions**

Directive of March, 2004

- To specify the procedure of MA in direction ***of a lowering of this procedure for the applicant***

- ***Elaborated widely in favour of the making of generics***

  - ***which benefits from all the possible opportunities***

Directive of March, 2004

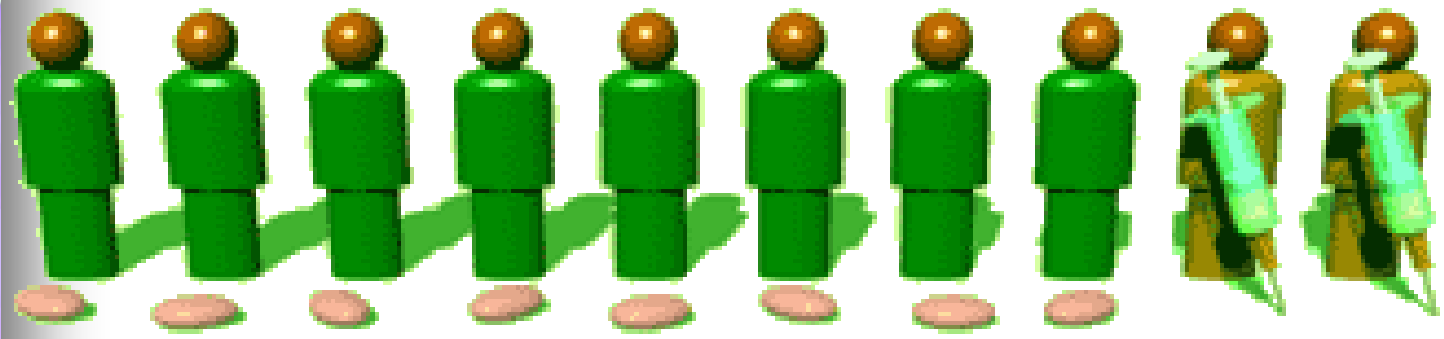
- ***Which has henceforth the possibility of asking the laboratory***
- ***making of the princeps to communicate ,***
- ***the file of MA which will be used to obtain the new authorization***

Directive of March, 2004

- ***It's not necessary for the laboratory making the generics***
  - ***To give the results of preclinical and clinical tests***
  - ***To give the file of MA for its generics***

The Executive Director of AFSSAPS can exempt studies of bioavailability in Human, to demonstrate its bio-equivalence with a referent special medicine

The MA file is then a simple duplication of the file of AMM as used for the reference medicine



Legal regime of generic medicines

- was built in such way to be ***the most flexible and the least forcing possible,*** for the actors
  - **(industrialists, public authorities)**
  - with considerable arrangements regarding the markets law and the possibility to get certificates to facilitate their development

Legal regime of generic medicines

- was built in inverse order:
  - the legislator stipulates the results to be reached
  - before the means are developed




Community MA of generics

- The criterion of safety, developed by the law of 1998 was not taken into account in the 2004 directives, in particular concerning excipients

- Too much forcing towards the development of the market
- This directive is more inspired by a market philosophy than by a sense of medical security

Community MA of generics and the precautionary principle??

It is a paradoxical attitude as far as we live in a society

which shows a zero tolerance for the " sanitary risks " (C.B)

Generic medicines or the consecration of the opportunism in public health (Sandrine Barthelmé) report

- **The commercial logic prevails over the sanitary logic**
- **The objective is not any more the patient but the cost cutting**
- **Prevalence of the commercial logic, justifies itself**
- **The strategies of the industrialists relieved by the economic incitements**

Incitement in the development of generic medicines

- The manufacturing of a generic medicine is interesting, the investment has to be profitable at short-term
- " The price of the princeps must be enough brought up so that the generics maker can have a sufficient profit margin in spite of the decline of the price "

Incitement in the development of generic medicines

- The princeps has to be a medicine enough prescribed to hope to increase the number of sales
- ***No generic medicine for the rare diseases or the orphan medicines***

Incitement in the sale of the generic medicines: the fixed price of "responsibility" (TFR)

- ***The TFR was conceived to give responsibilities to the patient, to trigger his awareness***
- **It consists in aligning the price of repayment to the price of generic medicine and,**
- **consequently, to make chargeable to the patient the additional cost of the leading medicine (set up by the Health Ministry , Douste Blazy in October, 2003)**

The stakes in the customized legal regime

The questioning of the precautionary principle as the foundation of the sanitary safety

Since the arrival of generic medicines modifications of the relationship maintained with the precautionary principle

- Precautionary principle: at the origin of German inspiration at the end of the 60s: principle recognised by the community law (EC Treaty 1992)
- In December, 2000, during the European council of Nice, extended to the health

Since the arrival of generic medicines modifications of the relationship maintained with the precautionary principle

- ***" New techniques of risk management the logic of which is to protect the community against a risk of damages "***

- It is an anticipative principle
- **In generic medicines, the precautionary principle has lost its intensity**
- It stays in recession with regard to economic interests

Generic medicines or the "revisited" precaution (C.B)

- **The apprehension of the notion of the risk conditions the dimensions of the precautionary principle**
- **In generic medicine, this apprehension is reduced to its simplest expression**
- **The generic medicines are the copy of a princeps, in principle without risks, explain the lowering of the procedure of M.A**
- **But excipients can vary between the princeps and its generic medicine and even between several generic medicines of the same molecule**

Distinguish the problems of " prescribability " and " switchability " prescription and replacement

- ***If we begin a treatment for a patient who has never received a given medicine, there should be only few problems because the posology can be adapted according to the wished therapeutic effect***
- Problem when we pass from a shape to another one,
- especially mattering for medicines with narrow therapeutic margin.
- In this last case, it is advised not to pass from a speciality to the other one (Folia Pharmacotherapeutica, Feb. 2006)

More problems of pharmaco-vigilance reported

- **to active principles in excipients**
- **to a bad traceability**
- **to modifications of bioavailability**
- **to confusions by the patient**
- **To a bad information of the patients and doctors**

In conclusion

- Be careful to excipients, coloring or other being able to lead to an allergic reaction
- The addition of an excipient or the change of a complex composition in excipients can raise problems especially in the case of chronic diseases well treated with the principal medecine
- The replacement can be at the origin of confusions

PRECAUTIONS

- ***Avoid the replacement for certain categories of population in particular the old and\or allergic persons***
- ***Avoid the replacement with medicines with narrow therapeutic margin***
- ***Avoid the replacement between generic medicines***

PRECAUTIONS

- **Improve the criteria of realization of the studies of bioequivalence IMPOSE THEM**
- **Privilege the replacement by generic medicines of composition and presentation identical to those of principal medicine princeps**
- **Privilege generic medicine devoid of excipients with notorious effect**

Common dangers for any medicines

- Impose a absolute traceability for the products of the blood, the meat of beef, the single-use materials etc.
- Impose the transparency of circuits
- Where does lovenox come from : of China, of USA ?
- Some originals can also be risk potentials

What to do ???

Legal references

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  Lawyer
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