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## Clinical research: a European Union Directive

Received: 5 December 2001  
Accepted: 5 December 2002  
Published online: 12 April 2002  
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A European Union Directive harmonising the different national regulations with regards to clinical research has recently been approved by the European Parliament and the Council. This is Directive 2001/20/EC of the European Parliament and the European Council, 4 April 2001, O.J., L 121/34. Biomedical research has hitherto not been regulated at the European level, and each country has its own corpus of laws and regulations. For example, the Netherlands has a law since December 1999, France since December 1988, Spain has a law for drug research only, and Belgium no law at all. The new directive concerns "the approximation of the laws, the regulation and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use." This ended a long process that had been initiated by the Commission when it issued a first draft on 4 September 1997. After a 3-year shuttle between Brussels and Strasbourg the Parliament gave its second reading on 12 December 2000, and the Council finally ratified the Directive on 4 April 2001. It is available on the website of the European Council (<http://www.europa.eu.int/eur-lex>).

The Directive must be interpreted in terms of the Commission aim to create a European internal market in which goods can circulate freely between the member states, in this case for medical investigational products. Basically, many provisions of the Directive are derived from the "good clinical practices" issued by and for the pharmaceutical industry for assessing new

The directive can be described as follows:

- It concerns only drugs trials, but it is most likely that many member states will take the opportunity to expand its scope to include all types of clinical research, including the nontherapeutic.
- It defines different roles for the investigator and the sponsor (usually a pharmaceutical company).
- It accepts a "single opinion" from one institutional review board per country.
- It allows the commencement of a trial after:
  - The favourable opinion of an ethics committee.
  - The authorisation from the states's responsible authority.

In addition to drug research sponsored by pharmaceutical companies, the Directive also opens the door for recognition of academic clinical research, initiated and sponsored by hospitals, research institutes, universities and nonprofit research organisations. Academic clinical research aims at promoting physio-pathological research as well as finding new indications for drugs already on the market, and/or defining new or optimal strategies. Comparing drugs already admitted to the market is an important issue in terms of public health [1]. However, the industry, usually and understandably, is not very keen at funding such research [2]. The Directive makes clear that the experimental drug should be provided free of cost by the sponsor, which makes sense when it is an industrial firm, because it will make the profit stemming from the research that it promotes. In this regard, the Directive leaves an opening for the member states to foresee in their national regulations exceptional circumstances whereby the sponsor (if institutional) would be exempted from the obligation to provide the investigational medical products for free.

The most critical issue in intensive care these days is the nature and quality of consent granted by incapacitated patients. The directive permits research on such a highly vulnerable population under three conditions: (a) the research is related to the disease from which the patient suffers, (b) there is either a positive risk/benefit balance or no risk at all, (c) informed consent is obtained from the patient himself or his legal representative (it is noted elsewhere in the Directive that this legal representative must be defined in the national law). The good news here is that for this type of research – as in similar clinical conditions of mental incompetence seen, for example, in psychiatry, geriatrics, pediat-

rics and neurology – legislators will be forced to consider the issue of deciding who is the best representative for incapacitated person. The bad news, however, is that emergency research, when the patient is unable to consent, and no surrogate is immediately available, will be impossible or illegal, as noted recently in the press [3, 4]. It is also of note that the recent update of the Helsinki Declaration (Edinburgh, October 2000) dropped the distinction between research with and research without direct benefit to the patient (World Medical Association, <http://www.wits.ac.za/bioethics/helsinki.htm>), at odds with some national laws that incorporate presently such a distinction.

Member states must implement the Directive within 2 years. It is our responsibility and that of our Society to explain these issues and to propose relevant solutions to politicians in each of the member states. The European Society of Intensive Care Medicine has created a task force which will make proposals at its next annual meeting in Barcelona (secretary: F. Lemaire, [francois.lemaire@hmn.ap-hop-paris.fr](mailto:francois.lemaire@hmn.ap-hop-paris.fr)).

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