Intensive Care Med (2004) 30:335
DOI 10.1007/s00134-003-2089-0

Christiane Druml
Ernst A. Singer

The European Directive: a further blow to science in intensive care medicine in Austria

Received: 25 July 2003
Accepted: 31 October 2003
Published online: 19 December 2003

Today's clinical trials lead to the therapies of tomorrow; without these we would have no safe and efficient treatments. Conducting clinical trials involves adherence to a number of strict rules (established in the "International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use," E6), including the obligation to obtain informed consent from each participating individual. However, obviously there are several groups of patients who are not able to give consent. The European Directive 2001/20/EC of 4 April 2001 states that these subjects can be included in a clinical trial only if informed consent of the patient's legal representative can be obtained. This is especially relevant for patients in intensive or emergency care medicine. It is obvious that a legal representative cannot be produced or consulted in these patient groups. However, no proven diagnostic or therapeutic measures can be developed for these patients without clinical trials. Instead of setting up rules to protect these vulnerable patients and their special needs the Directive does the opposite: the law prohibits research, hinders therapeutic progress, and thereby violates the Helsinki Declaration (provision 6: "... even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research...").

With regard to Austria the EU Directive is the cherry on top of another irritating legislation. The Austrian Medical Device Act (Medizinproduktegesetz BGBl, 1997/21, Austrian Law on Medical Devices) states that clinical trials with medical devices can be performed only if the patient has given informed consent. There are no provisions for exceptions [1]. This prevents any research being carried out in Austria that involves medical devices for emergency conditions or in the intensive care setting. It is truly disappointing that European legislation extends this unique Austrian peculiarity to drug research, neglecting values of solidarity. It is a very small consolation that provision 5 of the Introduction states that the notion of "legal representative" refers back to existing national law, thus opening loopholes for creative legal interpretation on the level of the member states. It seems, rather, that the European Commission has avoided discussion and has shunned responsibility in a serious and complicated matter. It would have been much healthier and more forthright had a pan-European solution been laid down.

The current requirements in Austria for the inclusion of temporarily incapacitated patients in drug trials are established in the 1994 Austrian Drug Act (Arzneimittelgesetz BGBl, 1994/104). The pertinent section of the act does not differentiate between critically ill patients in the ICU and those in emergency situations. However, proxy consent does not exist in Austria, i.e., family members are not automatically entitled to provide assent for the patient (exception: parents for their children). Thus with regard to temporary incapacitation two prerequisites necessary for the inclusion of an individual without prior informed consent are specified: (a) eligible patients can be included only if the ethics committee endorses the inclusion, and (b) if the investigator, due to his expertise and experience, is convinced that the expected benefit for the health of the patient due to his participation in the trial cannot be obtained by the administration of a registered medicinal product. The investigator must submit a patient information document to the relevant ethics committee, which is to be given to the patient as soon as he is able to consent and must contain basic information on the trial and the insurance (all drug trials in Austria require insurance to be effected in the patient's benefit). Taken together, current legislation in Austria does allow drug trials on temporarily incapacitated patients, while it is not at all clear whether such trials are possible under Directive 2001/20/EC.

Another difficulty is the "one single opinion." Article 7 of the Directive states that for multicenter clinical trials the member states shall establish a procedure "providing for the adoption of a single opinion for that member state." The Directive does not further specify this requirement but sets a time limit of 60 days for the vote. Until now many European member states have dealt with the incorporation of this article into national law in a very hesitant way, as the local committees fear losing control over the protection of "their" patients. They exert their influence to keep matters as they are. In Austria there are currently about 40 ethics committees. Their request to see and judge all documents of a planned multicenter trial and to participate actively and substantially in the process of finding a vote is understandable but, on the other hand, at variance with the idea of the Directive and not realistic in the face of the 60-day deadline.

However, the most serious and general problem with the Directive is in academic research. The Directive's attempt to implement Good Clinical Practice in European law and to harmonize regulation is a failure [2]. Multinational clinical research on an academic level in Europe will *not* be facilitated. The number of bureaucratic requirements which must be fulfilled before a trial can start has increased tremendously. Academia does not have the infrastructure and—paid—human resources to prepare the necessary forms, copies, and other documents, which leaves publicly funded research clearly at a disadvantage. However, the pharmaceutical industry does have the necessary infrastructure.

Academically sponsored research in comparison to industrially sponsored research will be at a serious disadvantage as will be European research in comparison to research in the United States. It is to be expected that large clinical trials performed in the United States, undisturbed by national bureaucratic barriers, will continue to contribute to "state of the art treatment strategies" for all patients, while such a scenario may not be feasible for Europe. The political, financial, and administrative hurdles to conducting pan-European trials will remain in spite of the Directive's goal (provision 10) "to simplify and harmonize the administrative provisions."

References

1. Singer EA. Müllner M (2001) Implications of the EU directive on clinical trials for emergency medicine. BMJ 324:1169–1170
2. Anonymous (2003) Who is afraid of the European clinical trials Directive? Lancet 361:2167

C. Druml (✉) · E. A. Singer
Ethics Committee, Medical Faculty,
University of Vienna
and Vienna General Hospital,
Borschkegasse 8b, 1090 Vienna, Austria
e-mail: christiane.druml@akh-wien.ac.at

E. A. Singer
Institute of Pharmacology,
University of Vienna,
Währingerstrasse 13a, 1090 Vienna,
Austria