

Implications of the EU directive on clinical trials for emergency medicine

Many trials in emergency medicine will not be possible

A laudable attempt by the European Union to implement good clinical practice in the conduct of clinical trials on drugs for human use will, unless amended, make impossible a range of potentially life saving studies after May 2004.

Directive 2001/20/EC, adopted in April last year, is an important and comprehensive document.¹ It is a cornerstone of a Europe-wide harmonisation of the provisions governing clinical trials and can be expected to foster and facilitate multinational clinical research. It will be adopted by member states before 1 May 2003, and its provisions will be applied from 1 May 2004 at the latest.

Several articles in the directive deal with the protection of clinical trial subjects. Article 5 outlines the conditions for research in incapacitated patients unable to give informed consent. The article, however, is framed to address the needs of individuals who are incapacitated for long periods, many even permanently. A clinical trial can only be done if "informed consent of the legal representative has been obtained." This will be difficult in many emergencies—when a patient is suddenly and perhaps temporarily incapacitated.

In some countries, such as the United Kingdom, there appears to be no provision for a legal representative for incapacitated patients. This means the doctor in charge takes responsibility for entering the patient into the trial. The situation appears to be similar in Spain and in Norway. In the Netherlands consent may be given by the life partner, at least in acute emergencies. In Germany patients may be enrolled if it can be assumed that the effectiveness of a treatment appears to be unclear. In other countries such as Ireland and Austria the situation may be more difficult. Legal representatives cannot be produced quickly and usually do not even exist, since a healthy adult person does not need a legal representative. Therefore, many studies performed in emergency medicine will no longer be possible after May 2004.

Acute diseases such as cardiac arrest, major stroke, or severe trauma are major health burdens. How shall we assess the effectiveness of healthcare interventions in patients with such diseases in the future? The directive may not only affect unconscious people. Thousands of patients with acute myocardial infarction have been enrolled in clinical trials so far. Many of these have severe pain on admission and receive treatment with opiates: can they give informed consent, particularly those with cardiogenic shock? Research in the acute care setting is already difficult and this directive will make it even more difficult.

The provisions of article 5 draw a sorry parallel to current legislation in Austria regarding the clinical testing of medical devices. Article 49 of Austria's Medical Device Act (implemented in 1996) states that any clinical study on a medical device can be done only if the patient has given her or his informed consent. At first sight, this seems reasonable and clearly in the spirit of the Helsinki Declaration. No provision exists, however, for a patient who is temporarily unable to

give consent. Consequently, any device designed for use in emergency situations, such as cardiopulmonary resuscitation, cannot be used in a clinical trial anywhere in Austria.

This legislation has created the absurd situation that a modern, industrialised country, loyal to the ethical principles of the Helsinki Declaration, leaves research and testing of medical devices to other countries. Austria is ready to use it only after clinicians and patients in other parts of the world have taken the risk of researching the intervention. Outside a clinical study, however, physicians are legally permitted to use any medical device if they think it is best for their patients. It seems barely credible that any legislation can create such an illogical situation for patients and their doctors.

Until now this situation was believed to be an alpine peculiarity, waiting to be amended as soon as the new European Union directive 2001/20/EC was incorporated into national law. Austrian researchers hoped that this directive would bring about the necessary changes in their Medical Device Act. Their hopes are now dashed, as Austria's affliction spreads into a European disease. It is unethical to create a Europe behind walls, which leaves others to solve research problems and then makes use of their work.

A solution to this sorry situation should be a quick amendment of the directive. The alternatives, such as alternative interpretations of the new regulations: and civil disobedience, do not appear to be an acceptable way forward. We should remember that provision 6 of the Helsinki Declaration requires that "Even the best prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility, and quality." Directive 2001/20/EC has undoubted merit and deserves respect, but it must set the rules for research in all clinically important situations and not hinder such research. Or should we simply deprive all acutely incapacitated adults of the benefits of proper research in the future?

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MM is involved in several research projects in emergency medicine where most patients, not only the unconscious, are temporarily incapacitated.

- 1 Directive 2001/20/EC of the European parliament and of the council of 4 April 2001 on the approximation of the laws, regulations 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. *Official Journal of the European Communities* 2001;L121:34-44 http://europa.eu.int/eur-lex/en/lif/dat/2001/en_301L0020.html [accessed 11 March, 2002]
- 2 Visser HKA. Non-therapeutic research in the EU in adults incapable of giving consent? *Lancet* 2001;357:818-9.