Squeezing academic research into a commercial straitjacket

New EU regulations for clinical trials come into effect this week. **Susan Mayor** talks to academics about the danger they pose to research

A new European directive on clinical trials that takes effect this week may seriously damage academic medical research by applying a "one size fits all" approach to the organisation of clinical trials that is more suited to trials designed for the registration of new drugs by pharmaceutical companies.

The aim of the European Union Clinical Trials Directive (2001/20/EC) was to harmonise the approval and monitoring of clinical research in different countries in Europe and to set pan-European standards of protection for all participants in clinical trials. It requires that all trials have a single sponsor, who carries full responsibility and liability, including covering the costs of all drugs or devices used in a study. This concept is familiar to commercial clinical research, where a pharmaceutical company is generally the sole sponsor of a trial. However, publicly funded research studies have previously generally operated as collaborations in which partners oversee different aspects of a trial.

Rory Collins, British Heart Foundation professor of medicine and epidemiology at the University of Oxford, explained the problem: "Many non-commercial research funders, universities, and hospitals are unlikely to accept formal responsibility in the new 'corporate sponsor model' because they do not have the necessary infrastructure or resources to undertake all the specified responsibilities."

The directive will also require more complex monitoring of adverse reactions to study treatments and verification of data in which the sponsor's role cannot be delegated to trial investigators. Professor Collins argued: "How can a non-commercial organisation—such as the University of Oxford or a medical charity—funding a multicentre trial take full responsibility for the day to day activities of a research centre in another country without a huge increase in costs?" He considers that current safeguards for trial organisation, including reviews of trial conduct, data quality, and pharmacovigilance by independent data monitoring committees have been sufficient to ensure the wellbeing of trial participants and the validity of trial results.

The fundamental problem with the new directive is that it was initially drafted as a way of facilitating the commercial development of drugs, based on consultation with the pharmaceutical industry. The needs of non-commercial research were considered only at a late stage.

Professor Collins warned: "The bureaucratic hurdles and extra cost will have a destructive effect on clinical trials. They will mean that some—maybe many—clinical trials will not be done. The fixed budget for academically funded research must mean fewer questions will be answered reliably."

The directive will be particularly damaging to clinical trials designed to assess the effect and the best ways to use drugs that have already been licensed, Professor Collins suggested. "These are not early-stage drug trials but the trials that assess the things doctors are already doing." One example is the heart protection study, one of the largest trials ever done to evaluate the impact of cholesterol lowering therapy and antioxidant vitamin supplementation in people at increased risk of heart disease. "Other casualties would be trials designed to assess different combinations, regimes, timings or intensities of cancer therapies, trials of steroids in head injury," he warned.

Terje Pedersen, head of the centre for preventive medicine at Ulleval University Hospital, Oslo, Norway, and principal investigator of the Scandinavian simvastatin survival study (4S) agreed: "The directive will make it even more difficult for a small country such as Norway to sponsor independent clinical trials that have important clinical impact." He added: "Smaller scale trials with relatively low budgets will be more difficult to organise. The main problem is going to be escalating costs for fees for inspections and monitoring."

Regulatory authorities in some countries have been working with non-commercial research organisations to develop national regulations that accommodate their needs. Although the directive was adopted in 2001, member states had to incorporate it into domestic legislation by 1 May 2004.

In the United Kingdom, organisations funding clinical trials, including the Medical Research Council and Cancer Research UK, worked closely with the regulatory body, the Medicines and Healthcare Products Regulatory Agency, to agree that UK regulations would not change the civil liabilities of the NHS, universities, or others undertaking clinical trials under the new European directive. The concept of co-sponsorship of trials with shared responsibilities will continue.

However, many countries have been slower to realise the potential problem. Professor Pedersen reported that there had been little discussion about the directive in Norway, although a meeting between researchers and trial regulators was held on 26 April. France and Germany are also likely to be late in incorporating the directive into national legislation. Other countries, including several Scandinavian countries and Italy, have largely adopted the directive because they had little existing legislation in place. Some countries had no choice—the newer members of the EU, mainly in eastern Europe, were obliged to implement the directive as a whole.

Professor Collins considered that even though some countries may have adapted the directive to suit academic research, this would not cover sponsors running trials in countries that have adopted it as it stands. "This may mean that it is not possible to include certain countries in clinical trials, so they may potentially miss out on the direct benefits this may bring to the patients involved and to medical education as a whole," he suggested.

The MRC is planning a conference this autumn to try to achieve an agreement across Europe that the UK approach to shared sponsorship of academic trials can be used in all countries. Dr Peter Duke, responsible for the MRC's policy on the directive, said: "We want to get clinical trialists around the table to share their experience on the best way to run trials with European regulators, with the aim of getting them to understand how multipartner, academic trials work on the ground." □

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Professor Rory Collins: "The bureaucratic hurdles and extra cost will have a destructive effect on clinical trials"

Aspects of the European clinical trial directive that may pose problems to academic researchers

- The requirement for a single sponsor—this does not fit the collaborative approach to sharing of responsibilities in multicentre publicly funded trials
- The introduction of rigid approaches to monitoring and pharmacovigilance—this may not be appropriate in many trials of marketed drugs
- The burdensome authorisation process
- The threat to important trials of emergency treatments in patients unable to give consent
- The increased costs of conducting trials—this, in conjunction with the limited public funds available, will inevitably result in fewer trials being funded

(Source: www.mrc.ac.uk)

The directive can be seen at www.europa.eu.int/eur-lex/en/search/search_lif.html