Differences in interpretation of the Directive's principles during implementation into national legislation have also led to differences in definition of what is, for example, an 'investigational medicinal product', a 'non-interventional study' or a 'substantial amendment' with the related handling differences. And as a lot of national requirements are only available in local languages on the Internet the organisation of a multinational trial is a real challenge requiring considerably more staff and hence financial resources than before.

Nearly every respondent in the ICREL survey agreed that the Clinical Trials Directive is aiming in the right direction. But we need to find ways to improve the systems and guarantee the same requirements for trial authorisation and performance in all Member States. Only then will we ensure the original goals of better patient protection, higher attractiveness of clinical research in Europe and faster drug development will be achieved. This may need improvement of existing and the development of new legislation. A decision on the next legislative steps can be expected in 2010.

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HEALTH DATA

'Nul points' for EU harmonisation of clinical trial ethical approval procedures

Getting approval for a multinational clinical trial is still time consuming and expensive, despite EU legislation in 2001 to promote good practice [1]. An article in the *British Medical Journal* by Andreas Schnitzbauer and colleagues [2] relates their experiences of an investigator-initiated trial in 10 European countries and three non-EU countries with a total of 40 sites in the EU and four sites outside the EU. The trial approval process started in July 2006.

Table 1: Time taken to get ethics committee approval and fees charged (2006–2007)

Country	No. of committees	Median no. of days (range)	Median charge (Euros)	Minimum (Euros)	Maximum (Euros)
Austria	2	35 (26 to 44)	0	0	0
Belgium	3	119 (119 to 181)	1,250	300	1,250
Finland	1	47	400		
France	1	123	0		
Germany	14	43 (29 to 93)	400	0	600
Italy	7	61 (35 to 107)	2,400	0	6,000
Netherlands	2	91 (61 to 120)	0	0	0
Spain	2	75 (72 to 77)	632	632	632
Sweden	2 *	30	1,460	1,000	1,920
UK	4 ◆	246 (192 to 266)	0	0	0

* simultaneous approval; ◆ national + local

The main difficulties involved time and money (see Table 1). The time taken for approval ranged from 30 days (Sweden) to 266 (UK). The UK required the most substantial changes, adding up to 100 days in response times from the study team (not stated in the table). However, queries from Belgium and the UK were regarded as most helpful in improving the study. Fifteen committees made no charge for their work, while in Italy five committees charged over Euros 2,000.

Forty-six per cent of ethics committees had queries about the insurance, even though certificates were obtained from an international broker in accordance with the national requirements. Countries that required submissions to local committees did not comply with the European law. Although the approval process led to constructive protocol modifications, the time taken affected study recruitment, which is critical in a trial with limited financial and human resources. Striking the optimal balance between turnaround times and identifying important critical ethical issues is essential to ensure clinical trials in the EU are safe and cost-effective.

Andreas Schnitzbauer and colleagues suggest that factors such as the use of a single language (English) for protocols and communications, standardising ethics fees, and centralising the review process, perhaps to an EU committee, may help achieve harmonisation.

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