Should trainees conduct research to assess the effects of drugs on patients?

The world of drug trials has changed dramatically in recent times. In the past, it sufficed to pose a clinical question (for example: 'Does morphine cause less postoperative nausea and vomiting than fentanyl?'), then formulate a proposal for prospective evaluation. Subsequent submission of this proposal to ethics and then research and development committees was usually relatively straightforward, such that it was often possible to start a project within 3 months of formulating the original idea.

Clinical trial regulations

Not so today. The European Trials Directive has been implemented into UK law, requiring trials to be designed and conducted in a similar manner to those undertaken by pharmaceutical companies, but with a fraction of the manpower. In the current climate, more stringent regulations over clinical drugs trials are to be expected and also applauded.

Recent media coverage of the trial carried out at Northwick Park Hospital involving the monoclonal antibody TGN 1421 and the conduct of drugs trials in the third world (Iheanacho, 2006) has highlighted the issues of safety and ethics at the forefront of public consciousness. Under the new regulations, hospital trusts and academic centres have a new role of 'sponsor', with final overall responsibility for trial design and conduct. As these organizations are still getting accustomed to the new regulations, they may be inclined to implement new rules during the ongoing planning and conduct of any trial, in order to avoid potential retribution for problems and complications resulting from clinical research.

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The net result of all of this is that it may now take a very long time to process a trial application and then begin recruiting patients. This is borne out by the author's experience, who while working in a 12-month half-time research fellow post, proposed a prospective randomized trial for a new analgesic.

A 9-month period lapsed from the original submission of the trial protocol for ethics approval to finally receiving permission from research and development to proceed with patient recruitment. This was despite a rapid response from the ethics committee as a result of the 60-day time limitation placed on them by the new regulations. The protracted consideration period was largely the result of the need for multiple applications to a variety of other regulatory bodies and inevitable delays while these applications were processed. The applications involved included:

- Sponsorship application to the trust
- Application to the trust research and development body, revised several times at their request
- Insurance approval to cover non-negligent harm to patients
- A revised contract with the pharmaceutical company supplying the treatment (also at the request of the trust research and development).

This particular application was not limited by a requirement for clinical trial authorization from the Medicines and Healthcare products Regulatory Agency, as the proposal was covered by an 'old' authorization (known as Doctors and Dentists' exemption, or DDX). But, if (as in most cases) the applicant holds no old DDX, then an already lengthy process will be prolonged further. Finally, clinical trial authorization applications under the new guidelines will only be considered after sponsorship by the trust has been approved. Trust sponsorship approval is lengthy by itself.

It should be noted that trials on volunteers, and studies assessing anything other than the safety and clinical efficacy of drugs, tend to require much less paperwork, and thus applications may be processed more quickly (Office of Public Sector Information, 2004).

Conclusions

One can see that it is quite possible that a trainee in a 12-month research post may not have time to recruit even the first patient into their proposed trial. It may still be worth embarking on setting up a new proposal, in such cases where the research group involved has a strong track record of continuous clinical research, and where it is assured that someone will take over the project once the trainee has returned to clinical medicine. However, it can be seen that in the course of a short research post, a trainee is more likely to be involved in the conduct of clinical trials that have been proposed by their predecessors than in their own proposal.

In the author's view, provisions should be made by Royal Colleges and the Postgraduate Medical Education Board (PMETB) to ensure that supervisors in the UK will be aware of the length of time required for the set-up of trials assessing drug safety or efficacy. Further, that the responsibility for a trial is only offered to trainees in combination with realistic information on preparation times. In the (far) future, 'clinical research facilities' may support investigator-led studies and change the overall outlook for trainees doing this form of research. **BJHM**

Iheanacho I (2006) Drugs Trials – the Dark Side: This World. Review. *BMJ* **332:** 1039

Office of Public Sector Information (2004) *The Medicines for Human Use (Clinical Trials) Regulations 2004.* The Stationery Office, London (www.legislation.hmso.gov.uk/si/si2004/20041031.htm)

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