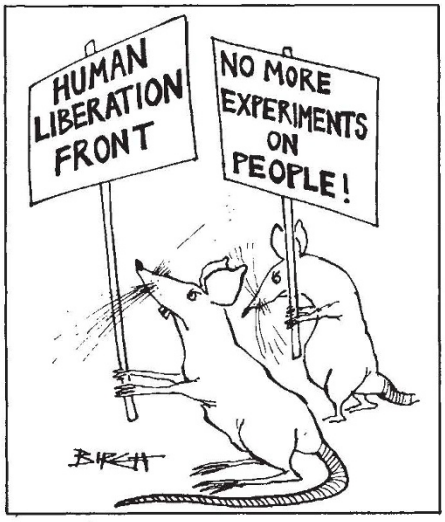
UK drug trials

Row over student trial

EVENTS have forced the British Medicines Commission into an urgent study of arrangements for testing new drugs on healthy volunteers. The issue has come to a head in the wake of complaints that plans for testing a new antitumour drug among London students are ethically objectionable and pay scant attention to the safety of the volunteers.

The disputed study, begun some months ago but now abandoned, was being carried out by a company known as Charterhouse Clinical Research Unit Ltd, on behalf of the manufacturer, Ortho-Cilag Pharmaceuticals Ltd. Volunteers, mostly students,



were paid £250 to be given 20 consecutive doses of up to 450 mg of hydroxyphenylretinamide (HPR), an analogue of vitamin A shown to be a tumour inhibitor in animals.

The study, designed to provide information of toxicity in human beings, has been criticized on the grounds that volunteers were not fully informed of the risks and that the testing company had failed to make adequate arrangements for monitoring participants' health. Inevitably, the result has been to reopen the contentious question of how clinical data on the effects of new drugs should be gathered — and of the role of academic pharmacologists in the process.

Under present arrangements in Britain, drug studies with healthy human volunteers are regarded as a private matter between consenting adults — the drug company and the volunteers. Since 1981, manufacturers have not been required to seek advance approval from the Committee on the Safety of Medicines (established, like the Medicines Commission, under the 1968 Medicines Act). One result has been the emergence of a number of companies linked with academic departments to provide human toxicity testing as a service to pharmaceutical manufacturers.

The whistle seems to have been blown on the Charterhouse trial by Professor Brian Rabin, professor of biochemistry at University College, London, who says HPR may plausibly accelerate the growth of some tumours, and who complains that Charterhouse had provided no information to the volunteers' own physicians and that it had no plans to follow up its volunteers to detect long-term untoward effects. He also attacks the information sheet given to volunteers for failing to list all possible side-effects of HPR and says the silence of Charterhouse's consent form on the matter of compensation in the event of damage being suffered is "totally disgraceful".

These criticisms are rejected by Professor Paul Turner, an adviser to Charterhouse and director of clinical pharmacology at St Bartholomew's Hospital Medical College. He says that "ill-considered remarks" and "destructive press coverage" have severely impeded research on a promising anti-tumour drug "showing no signs of toxicity".

Turner says that Charterhouse accepts work only on the condition that a written indemnification against damage claims is provided by the client company. A new consent form being drawn up by Charterhouse will aim to comply with a recommendation of the Association of British Pharmaceutical Industry that no-fault compensation should be offered explicitly to volunteers. Turner argues that new drugs such as HPR are best tested in an independent company separate from the manufacturer.

Although the HPR study had been approved by Charterhouse's own ethics committee, the deans of the London medical schools have now recommended that their students should take part only in studies that have been subject to independent scrutiny. Under a new agreement between Charterhouse and the Metropolitan Conference of Medical Deans, studies on students will in future be approved by the ethics committee of St Bartholomew's Hospital, with which Charterhouse is closely associated.

Although many British pharmaceutical manufacturers have in-house testing units, more and more volunteer studies have recently been carried out by small independent companies, often associated with pharmacology departments in medical schools, whose earnings can provide a welcome source of research funds. Charterhouse Clinical Research Unit Ltd was set up by Synthelabo, a non-profit charity linked to St Bartholomew's Hospital Medical College.

The demand for volunteer studies has grown rapidly since the introduction in 1981 of the Clinical Trials Exemption Scheme, which allows manufacturers with a good case for a drug to go into clinical trials without first facing a full-length scrutiny by the Department of Health's Committee on the Safety of Medicines. It is widely believed that a good volunteer study increases the chances of an exemption certificate being granted.

Practice varies from one company to another: some, such as Drug Development (Scotland) Ltd, linked to the University of Dundee, routinely notify volunteers' physicians about studies. Dr John McEwen, the company's medical director, says that information from volunteers' physicians has often proved useful to those running the studies. The company also offers no-fault compensation in the event of claims for damages, and is insured to cover any claim.

The Medicines Commission, which advises the government on matters related to medicines generally, now has some difficult questions to face. Members will certainly be mindful of Professor Turner's warning that if drug development is hampered in this country, the big manufacturers will simply pack their bags and go elsewhere.

Manufacturers feel hard done by because more is expected from them and from their pharmacological agents than from academic researchers in, say, physiology. Thus in the event of harm to a volunteer in an experiment by an employee of the Medical Research Council, the council would offer an *ex gratia* payment but there would be no legal redress unless negligence could be proved. The voluntary code on compensation to which most commercial companies adhere commits them to damages in a way the Medical Research Council and the Department of Health have been unwilling to apply to themselves.

Tim Beardsley

France seeks rules

THE testing of new drugs in France is to be tightened up, in a move by the ministry of health. No precise bill is yet on the table, but a "draft project" is under study, according to the French evening newspaper *Le Monde*.

French law on the matter is obscure, with some experts claiming that human tests are totally illegal. Testing has nevertheless been carried out, but often in a clandestine and unsatisfactory manner, making France — according to some — an effectively liberal regime in which multinationals can conveniently try out new formulas.

According to the ministry's draft, however, subjects and the authors of trials should sign clear written agreements with each other; payment should be according to published terms; authors would have the burden of proof; and prisoners, or members of the author's staff, would not be used as subjects unless it would be to the benefit of their health. Further, all human trials would be subject to the approval of a regional ethical committee — though the constitution of such a body remains, for the moment, undefined. Robert Walgate

0028-0836/84/060496-01$01.00