Britain: Drug trial leaves volunteers seriously ill

Scientist attacks lax regulatory regime

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29 March 2006

The drug trial conducted at Northwick Park Hospital, London, that left six volunteers seriously ill has prompted a medical researcher, Dr. Aubrey Blumsohn, to challenge the role of the British government's drug watchdog, the Medical and Healthcare Products Regulatory Agency (MHRA).

The six men were taking part in the initial, Phase One, trial of TGN1412, a drug produced by a small German pharmaceutical research company, TeGenero. Trials were contracted out to Parexel, a US-based company that operates in a number of countries.

Immediately after taking the drug the men suffered acute adverse reactions, described as massive inflammation, extreme pain and vomiting, slipping in and out of a coma and the beginnings of organ failure. They were immediately put into intensive care and whilst four are reported to be improving, two are still on the critical list two weeks later.

Drugs trials in Britain are supervised by the MHRA, which is financed by the pharmaceutical industry. Investigation of what went wrong in this drugs trial is also being carried out by the MHRA.

Dr. Blumsohn told the WSWS: "The question is, 'Who watches the watchdog?' Any proper investigation of this tragic matter would seem almost by definition to involve the MHRA as subject of further examination rather than as investigator."

The British government is so keen to encourage investment by the drugs industry that it refused to accept the recommendations of a report prepared last year by the House of Commons Parliamentary Health Committee entitled "The Influence of the Pharmaceutical Industry." This report recommended that the MHRA should be made independent of the pharmaceutical industry. Specific criticisms raised in the report concerning drugs trials include: "Limited information given to trial participants" and "Exposure of participants to unacceptable risks."

As well as the lax regulatory regime, the drug trial highlights the way the British government is encouraging private involvement in the state-run National Health Service (NHS). Northwick Park is an NHS hospital but Parexel has a 36-bed unit within the hospital, relying on emergency treatment provided by the NHS.

Parexel are allowed to advertise for volunteers for their trials, stating that recruits will be "paid for your time and inconvenience," despite drug industry guidelines stating that payments should not be mentioned in public notices. Press reports reveal that volunteers took part primarily because of the £2,000 fee they would receive for about two weeks spent in hospital.

Regarding the TGN1412 trial, Dr. Blumsohn said, "Participants in trials do knowingly subject themselves to risk for financial gain or for altruistic reasons. What is not known is whether the research design was appropriate, whether those risks were properly evaluated, whether the degree of risk was conveyed honestly to participants, and who is responsible for this. The MHRA would have been in large part responsible for considering the strength of evidence underlying both the appropriateness of human trials and the trial design. Simultaneous study of six individuals in the first human trial of a drug would seem to constitute poor study design under any circumstances."

Dr. Blumsohn pointed to comments made in the *Sunday Times* about the drugs trial. TGN1412 is not a

traditional chemical product but a “monoclonal antibody,” a protein that is genetically engineered to target cells in the body’s immune system. Most monoclonal antibody drugs are designed to suppress the immune system’s reaction. There are now several such drugs on the market, including Herceptin, the breast cancer drug.

TGN1412 is unusual in being designed to stimulate production of so-called T-cells that regulate other cells in the immune system. According to experts the danger is that rather than stimulate the regulators it is possible to overstimulate the entire immune system, which is what seems to have happened in this case.

Professor Angus Dalgleish, a cancer specialist at London University and world expert on the immune system, told the *Sunday Times*, “I would have told the people doing this trial not to do it because the dangers were so great.” Citing earlier studies on similar drugs that had caused severe side effects, he said of the researchers, “They should have known they would get a meltdown because this drug was hitting exactly the same immune response pathways.”

A similar comment was made by Jorg Schaaber, a member of the German drug industry monitoring group Buko Pharma (referred to in the novel *The Constant Gardener* by John Le Carré). Schaaber said that all trials of monoclonal antibodies had shown the drugs carried “considerable risks” of side effects and that “anyone getting involved in these studies should be made aware of that.”

Dr. Blumsohn has a particular concern over how the pharmaceutical industry conducts its research. Universities in the main are now reliant on grants from the industry for their investigations, and he was suspended from Sheffield University last year after challenging Procter & Gamble Pharmaceuticals for not giving him access to statistical data on research that he had carried out on osteoporosis drugs.

He commented on the MHRA in the present case: “They are investigating themselves. It is all completely implausible and the whole regulatory system is a house of cards that is about to fall over.”