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Occupation: lab rat

Thousands of people make their living scurrying from one clinical drug trial to the next. Are they risking our health as well as their own, asks **Alison Motluk**

OLIVER is feeling tired on the day I call. I assume it's because he's been sleeping on a narrow bunk in a room with five other men, or because he has to get up at 7 am to give blood samples. Or that he hasn't been outdoors in two weeks. He doubts it – that's all just an ordinary part of his working life.

Oliver* is a professional guinea pig or "healthy volunteer". When we speak, he's in Austin, Texas, taking two different HIV drugs in combination over 20 days. At the end he'll receive $5000. Before this, it was an injection of a cancer drug in San Antonio. "My lymph nodes got swollen and tender but it went away a week later," he says, but it was well worth it for $2800. In January, he pocketed $3000 for a 10-day stint testing an antibiotic (which made him vomit) and in October 2008 he was in Dallas for 32 days to test a liquid anti-cholesterol drug. For that he raked in $9100. In total last year, he earned $34,000 as a therapeutic guinea pig.

The 32-year-old former hotel manager is just one of tens of thousands of people around the world who make a living out of participating in clinical trials (see "Guinea pigs 'R us", page 43). Officially they are "volunteers", paid only for the inconvenience of giving up their time for science, but with rewards of up to $300 per day in the US or around £150 per day in the UK, many sign up for one trial after another, and consider themselves fully employed. As long as they stay healthy enough to be accepted for the next trial, they can make a decent living out of taking pills, allowing blood to be drawn and spending night after night in testing facilities.

While the money can be good, this is potentially dangerous work. Nearly all the studies that recruit healthy volunteers are "phase I" trials – the first human safety evaluation of a drug that has previously only been tested in animals. They can, and sometimes do, go awry (see "A dangerous occupation", page 42"). As a result, such clinical trials tend to attract the unskilled, unemployed, and people who need fast access to cash. Students, people with debts to pay and, according to Oliver, a fair number of convicted felons are common volunteers. There have been reports of illegal immigrants, homeless people and alcoholics being signed up as human lab rats.

Now some health researchers and bioethicists are expressing concern at the way socially and financially vulnerable people are being drawn to careers – full-time or otherwise – as guinea pigs in phase I clinical trials. They point out that offering financial incentives to test new drugs and treatments puts the poorest members of society unfairly at risk. Furthermore, offering substantial sums to human lab rats could be producing misleading data that might allow unsafe treatments to reach the market.

One problem is that the need to earn money can encourage volunteers to flout the rules ›

* names have been changed

created to protect them, as well as affecting the quality of the data. Most trials, for example, insist on a 30-day minimum drug-free period before the study begins, but since there is no system in place to check this, and plenty of financial reasons to ignore it, some volunteers may show up at the next trial before this 30-day "wash-out period" is up. This not only means that volunteers could be loading their bodies with potentially dangerous combinations of drugs, but also that unforeseen side effects of these cocktails could skew the results of the second trial.

Despite these risks, the temptation to ignore the rules is strong. Career volunteer Brandon, who is living in his car between trials, says that he regularly flouts the 30-day rule. He claims he cannot afford to take a month out when a trial comes to an end. "Break means broke," he says.

Another concern is that the pressure to maximise income may influence what volunteers admit to whilst on the trial. Some side effects, for instance, can get you kicked out of a study early, and since most of the payment is made upon completion of the trial, reporting side effects can be costly. Other times it might pay to fake side effects so you can drop out and sign up for another, more lucrative trial. Either way, being selective with this kind of information can skew the results of a clinical trial. "It's so crucial that the data are accurate," says Adil Shamoo, a biochemist at the University of Maryland in Baltimore and founder of Citizens for Responsible Care and Research. Bad reporting puts the public at risk, he says.

"Millions of subjects are up a creek if they're injured. It's one of our biggest shames"

Last year, Shamoo published evidence that side effects in drug trials are indeed under-reported. Between 1990 and 2000, 386 adverse events and eight deaths were reported to the US Office of Human Research Protection, which governs human research using federal funds. Yet when he compared those numbers with annual data from the Food and Drug Administration on newly approved drugs, he found that each year nearly 17,200 adverse events were reported, with 800 serious problems including death – even though the FDA data applied to a sample population one-third of the size (*Clinical Pharmacology and Therapeutics*, vol 84, p 275).

While payment clearly brings up many ethical and practical issues, bioethicists are divided on what should be done about it. Some argue that the money on offer should never be enough to induce someone to do something they would not otherwise do. Others think that is naive: why would a healthy person take a cocktail of drugs and live in confinement for three weeks for any other reason?

Bioethicists Carl Elliott at the University of Minnesota in Minneapolis and Trudo Lemmens of the University of Toronto in Canada think it is time to face up to the fact that drug testing is employment and, as such, should be subject to inspections to make sure working conditions are safe (*American Journal of Bioethics*, vol 1, p 51). They and others, including Shamoo, go so far as to suggest that professional guinea pigs ought be unionised and in countries like the US, where healthcare is not provided by the state, should be offered health benefits. At present, this is something volunteers are not entitled to even if something goes wrong. "Millions of subjects are up a creek if they're injured," says Shamoo. "It's one of our biggest shames."

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Peter Lurie of Public Citizen, a consumer advocacy group based in Washington DC, disagrees: he doesn't think people should be making a living as lab rats in the first place. "Somebody who is supporting themselves exclusively this way is somebody we should be worried about," he says. He feels that it's wrong that a small number of people of a certain income level should bear the burden of keeping pharmaceuticals safe. "The risks need to be spread out between men and women, rich and poor, old and young," he says.

Ethics for sale

Others feel that the problem lies not in the financial rewards offered to volunteers, but in the lack of oversight of privately run clinical trials, particularly in the US. And while trials used to be run mainly by universities, whose good name – and sources of funding – were at stake if they acted less than ethically, most are now run through commercial contract research organisations, whose reputations depend primarily on being quick and hassle-free, having plenty of subjects at the ready, and generally assisting pharmaceutical companies to speed a drug to market.

In the US, not only have clinical trials gone commercial, so too have the ethics boards set up to oversee them. American ethical review boards, known as institutional review boards (IRBs), were designed back when most research was done in a university setting; they were made up of other researchers from the

A dangerous occupation

In most medical trials, side effects are nothing more serious than rashes, sleepiness, loss of appetite or constipation. Sometimes, though, human guinea pigs find themselves on the sharp end of a potentially life-threatening adverse reaction.

One of the best-known cases is the phase I trial of the monoclonal antibody TGN1412 in London three years ago. Shortly after receiving their first infusion of the drug, which stimulates the body's T-cell immune response, six healthy volunteers were taken to intensive care suffering from multiple organ failure. None died, but one lost several fingers and toes. Questions remain about their long-term health.

In an unconnected incident five years earlier, Ellen Roche, a healthy 24-year-old lab technician at Johns Hopkins Asthma and Allergy Center, inhaled hexamethonium, an experimental drug known to constrict the airways, and used to mimic the symptoms of asthma. The next day she developed a cough and shortness of breath. She went on to suffer respiratory distress and multi-organ failure. She died soon afterwards. The internal report of Johns Hopkins University School of Medicine, where the trial took place, concluded that Ellen's death was "most likely the result of participation in the hexamethonium phase of the experiment".

university. But now the great majority of drug trials in the US are reviewed by for-profit IRBs. With no stringent educational requirements for members, no formal government approval process for setting up an ethics board and limited oversight by government regulatory authorities – the FDA inspects only about 1 per cent of clinical trials – they are seen by many experts as the main problem. Indeed, IRBs are routinely – and legally – paid by the same drug companies whose trials they are supposed to be regulating. "IRBs have a financial interest in pleasing the people who write their pay cheques," says Elliott. "They have a built-in conflict of interest."

Indeed, in 2003, an investigation by the American financial magazine *Bloomberg Markets* discovered that one contract research organisation had for years been running clinical trials in a dilapidated hotel, using undocumented immigrants as guinea pigs. In other cases in the report, some IRBs approved trials that were overseen by doctors who had no licence to practise or had criminal convictions.

What's more, the open market for IRBs means that drug companies are able to shop around for the most lenient IRB they can find. This last point was driven home earlier this year, when the US Government Accountability Office submitted a fake proposal for trialling a high-risk surgical procedure. It was rightly turned down by two IRBs but was accepted by Coast IRB in Colorado. Notably, that IRB had not turned down any of the 356 proposals it had received over the previous five years. "That was alarming in every way," says Elliott. Coast IRB closed down at the end of June.

Yet despite the health risks and the lack of protection for volunteers, many human guinea pigs, including Brandon and Oliver, think that $30,000 a year for a job that requires nothing more than a body in good health is a pretty good deal.

In fact, when I caught up with Oliver again a few weeks after our phone call, the Austin study was over. He was in the middle of picking up a rental truck so he could move his stuff up to North Dakota, where he had been accepted into a new study on an Alzheimer's drug. He had hired two men to do the heavy lifting, though. "I'm not supposed to do strenuous exercise," he said, explaining that it could cause his liver enzymes to go up. "Places will exclude me if my levels are too high." ■

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Guinea pigs 'R us

Why would anyone take potentially lethal drugs for a living? For Oliver*, aged 32, a combination of a career crisis and a divorce in 2007 sent his life into a tailspin and saw him drinking heavily and failing to pay his bills. In January 2008, he signed up to test an antidepressant – his first clinical trial. "I had a $3000 debt and $400 in rent to cover," he recalls. The study paid for everything in 22 days.

For Brandon, the first time came about not as an escape but as an opportunity that sounded too good to miss. Four years ago he was in a bar when a friend came in and announced that he could earn $2500 just for mixing booze with painkillers. Brandon, then 29, signed up. He spent the whole trial throwing up, but he still says it was in many ways less humiliating than many of the restaurant, factory and warehouse jobs he's had over the years.

Many career lab rats get the lowdown on the trade through the website Just Another Lab Rat (www.jalr.org), created and maintained by Paul Clough, a professional volunteer. Clough estimates that there are about 10,000 volunteers in the US who can be considered professionals, in that they do three or four large studies per year and earn $20,000 or more.

Clough has been testing drugs full-time for almost five years, has spent about 500 nights in research facilities and had 3000 blood draws. Now aged 30, he expects to be in this line of work until he is 45 – an age at which he will automatically become ineligible for a large number of studies. In a section on his website called "Exit strategy", he encourages people to plan for this. Clough himself has already launched a business making balloon animals at festivals and corporate events.

Clough's website provides basic information about drug testing, such as what you can expect to be paid, what words like "double-blind" mean, and what kinds of studies are out there. He reminds people that it may be difficult to work all year round and that they may not get into every study they pursue.

He himself has been excluded from studies because of high blood pressure – ironically brought on by anxiety about not being accepted into the study. "It's especially bad when I really need to get into a study, when there's money riding on it," he says. It turns out this is fairly common, and Brandon was also recently disqualified for a trial for this reason. Clough provides tips to others on how to use deep breathing and relaxation to tackle performance anxiety.

Clough is frank about the risks too. "You will be taking an experimental drug that few or no humans have taken before. So, yes, there is a chance that you may become ill, have adverse side effects or possibly die," he writes. For career labs rat, however, the fear of the unknown is clearly trumped by the certainty of earning cold, hard cash.