

TESTING TIMES

for human research

How the pharmaceutical industry is striving to attract and retain volunteer patients for clinical trials. By **Julian Rogers**

Bringing a new drug to the market can cost up to US\$1 billion and take 20 years. Of this, clinical trials are the costliest and most time-consuming aspect of drug development. Once a drug has proved a success on animals in the laboratory, researchers have to test the medicine on its intended target – humans. However, if a clinical trial backfires then the knock-on effect for the industry is potentially catastrophic. Horror stories of human guinea pigs suffering severe, adverse reactions during trial drugs are hardly music to the ears of would-be volunteers. This is on top of the statistic banded around that one in four patients drop out of a trial be-

fore it finishes. Studies have also found that 30 to 40 percent of all clinical trials last longer than expected throughout all phases of testing due to patient recruitment delays.

It seems drug companies are fighting harder than ever before to attract and hold onto patients. Negative publicity only adds to their woes.

Early this year the industry was put under the microscope when a UK clinical trial ended in dire circumstances. Eight men were paid UK£2000 (US\$3670) each to test an anti-inflammatory drug, TGN1412, created by TeGenero. Six were administered with the drug, designed to treat rheumatoid

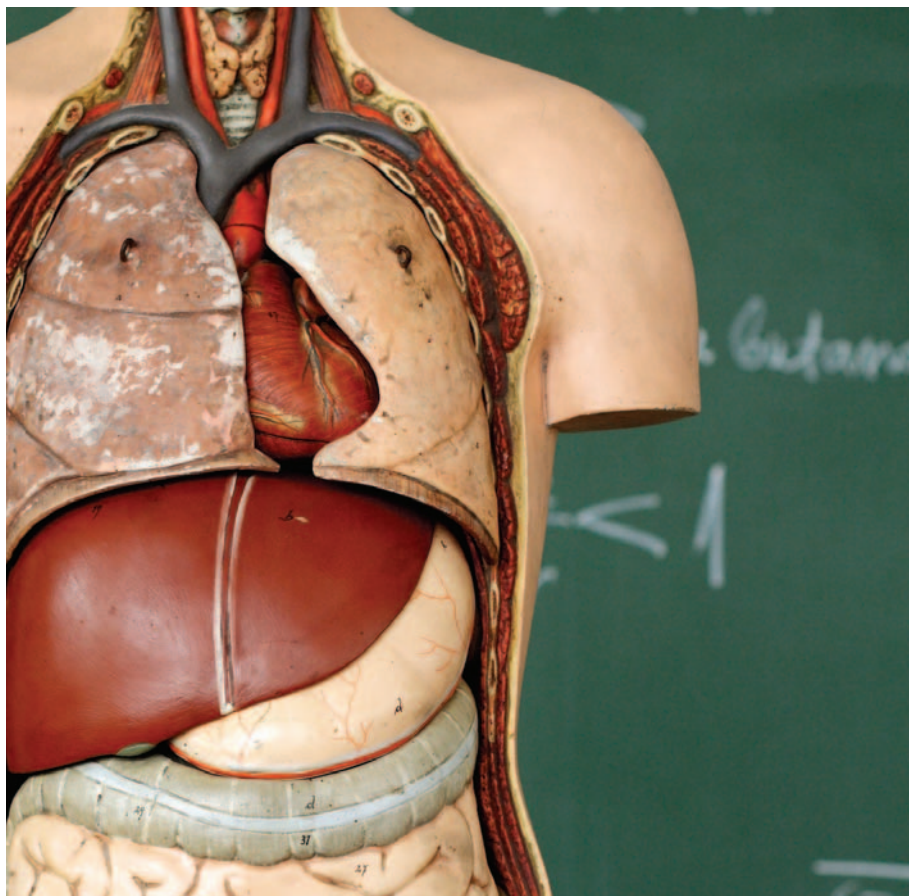
arthritis, leukaemia and multiple sclerosis, while the other two were given a placebo. Almost immediately after the drug was administered six of the volunteers suffered adverse reactions including severe swelling to the head and multiple organ failure. One of the men described how it felt like his brain was “on fire” shortly after being given the drug. Another volunteer, who was most affected by the trial, has since been told by doctors that he may lose all of his toes and parts of three fingers.

This was not the first trial to produce adverse reactions and it won't be the last. However, the incident put the whole procedure of clinical trials under the microscope in the UK and led to serious doubts being raised about clinical trial safety. TeGenero still maintains that the volunteers' reactions were “completely unexpected” and did not reflect the results of earlier tests on animals in the laboratory. The World Health Organization (WHO) has called for stricter registration of trials so that negative results cannot be kept behind closed doors. Currently researchers can opt to wait until they are well advanced in their work before releasing results.

Despite the uproar and negative publicity surrounding the UK trial, those within the industry in the US are in no doubt about the importance of testing drugs on humans. “Without people who are willing to participate there would be no process to test new medicines, vaccines, and devices,” asserts Dr Diana L Anderson, CEO/President of D. Anderson & Company – a patient recruitment and retention provider. “Thus, without testing on human subjects, there wouldn't be any new drugs made available to the public. Not only are clinical trials important in order to test the efficacy of new drugs and devices but they are a necessity based on the strict rules and regulations that are mandated by the FDA.”

Regulations

The struggle to get people through the doors at research centers has a detrimental effect on the time it takes to get a drug out on the market. In fact, it now takes nearly twice as long to develop a new drug as it did 30 years ago.





DR DIANA L ANDERSON

Nevertheless, a clinical trial that uncovers an unforeseen side effect is far better than if the drug was already on the market. Merck found this out to its cost when it was discovered that its painkiller drug Vioxx was linked to higher rates of heart attacks. Bosses argued that the drug, withdrawn last year, was thoroughly tested before it was released and was continually monitored once it went on sale. Merck has already paid out millions of dollars in damages as it faces a raft of lawsuits. The US drug testing industry is regulated by the FDA, which gives the green light as to whether or not a clinical trial can go-ahead. The lengthy and expensive process goes through three phases of testing before a drug is given approval. This takes several years and may include hundreds of volunteers. After the launch of the drug there is a safety surveillance period when the product is monitored for any rare or long-term side effects.

Ken Getz, Co-founder and Board Chair of the Centre for Information and Study on Clinical Research Participation (CISCRP), says that better communication is needed between drug trial firms and the public in order to educate people about the benefits of trials. He also believes the firms need to cut out the impersonal and monosyllabic statements when a trial goes wrong. “Typically, and I believe mistakenly, research professionals are instructed not to respond to negative and sensational media coverage. And, when required, their PR machines tend to provide very mechanical responses to human tragedies that lack heart and compassion.

As a result, the only communication and education that the public receives from the research community pertains to filling trials or stimulating drug consumerism.”



KEN GETZ

Information

CISCRP, a non-profit formed in 2003 to raise awareness of clinical trials, has been making great strides in educating the public and media about clinical trials. Although patients are paid for taking part and helping in the battle against serious illnesses, there still seems to be a stigma attached to human testing. Giving blood or donating an organ is seen as a more admirable thing to do in many people’s eyes, it seems. CISCRP also believes that a better-educated volunteer is more likely to sign up for further trials. In fact, 80 percent of volunteers never take part again once their trial is over – a harsh trend that the industry is desperate to reverse. “The clinical research community desperately needs to pro-actively educate and communicate with the public,” Getz notes. “This requires a long-term commitment to public outreach and advocacy. However, I do think that as an industry we must do a better job of generating awareness about clinical trials among the public by communicating all the positive benefits that come from participating in clinical research studies. There are so many good things to report and if we could mobilize our energies as an industry in that direction we could certainly promote a positive message that could have a major impact on public opinion.”

Another problem faced is recruiting participants from different ethnic backgrounds, according to Anderson. “Ensuring diversity in clinical research is important and in some cases mandated by the protocol. These groups vary based on ethnicity, gender, and age and include women, children, African-Americans, American Indians, Hispanics, Asians, and

others. Cultural sensitivity must be considered when recruiting from these populations and the messages must be clearly differentiated for each group with translations made available where appropriate.”

Reaching out to minority groups of society will continue to be an uphill task but Douglas Peddicord, Executive Director of the Association of Clinical Research Organizations (ACRO) says most people are not aware of what is involved with a clinical trial. “Surveys repeatedly show that the biggest barrier to recruitment is lack of knowledge about the importance of clinical trials and of opportunities to participate. More than ever, perhaps, it remains incumbent upon physicians and other medical pro-

A DRUG’S JOURNEY TO MARKET

Phase One

Initial testing is carried with a small group of volunteers (20-100) who are usually paid for their efforts. The trial is used to determine what happens to the drug in the human body – how its absorbed, metabolized and excreted. A phase one study will examine the side effects as dosage levels are increased. Testing is typically carried out over several months, while around 70 percent of experimental drugs will pass this initial stage of testing.

Phase Two

Once a drug has shown to be safe, it must be tested for efficacy. This phase may last from several months to two years and involve up to several hundred patients. One group of patients will be administered the drug while another group will receive a placebo. Often with these trials, the patients and the researchers have no idea who has received which drug. Only around one-third of experimental drugs complete both phase one and two.

Phase Three

A study at this stage of the process may involve thousands of patients, and provide the pharmaceutical companies and the FDA with a more thorough understanding of the drug’s effectiveness, benefits and possible adverse reactions. Phase three trials usually last years but 70 to 90 percent of drugs that make it this far complete this stage. Once complete, the pharmaceutical company request FDA approval for marketing the drug.

Source: Thomson Center Watch

professionals to be part of ongoing educational efforts to accurately and positively communicate the key role of clinical trials in facilitating the development of new drugs and new treatments for the people that need them.”

Anderson also suggests that patient recruitment processes are always different and retention programs should be planned accordingly. “When it comes to recruiting study volunteers we have discovered there is no ‘cookie-cutter’ approach to this and firmly believe that one size does not fit all. Therefore different recruitment and retention strategies must be planned and executed in order to ensure a successful outcome. A fully-integrated marketing approach may include advertising, the internet, direct-to-physician communication, training programs, community outreach, and care-giver support programs.” She adds: “These strategies can be very effective as time and budgets will allow. However, there are some studies that require a very select patient population group where a broad-based communications platform isn’t necessary or appropriate so recruitment strategies must be analyzed differently for each study.”

Outsourcing

But while the diminishing number of volunteers is proving a headache for the pharmaceutical companies and researchers, increasingly they are outsourcing human testing to the developing world. India, for instance, is flourishing as a clinical trials hotbed. As well as the cost savings of between 30 and 50 percent, the pharmaceutical firms are able to tap into a large pool of patients from multiethnic and multiracial backgrounds. Critics argue that volunteers are naive about the potential consequences of human testing and that some trials are illegal.

Anderson, however, hopes that this enthusiasm to participate will rub off on Americans. “Within the last few months I’ve been fortunate enough to travel to China and India as well as other emerging markets and I’ve seen first-hand the momentum and enthusiasm for clinical trials that is taking place in these countries. They have enormous populations and they are very willing to participate in clinical trials. I also hope and believe that as the general public here in the US becomes more aware of the benefits of participating in clinical trials that we will see greater levels of participation in the future which we will certainly need in order to meet the demand for all the new compounds that will be developed within the next 10 years. This is an exciting time to be in-

involved in the clinical trials industry and I’m very optimistic about our future.”

So while human testing will continue to be the most costly and time-consuming aspect of drug development, it is the only way that drug development can move forward. New medicines have to be tested on people to see if they work – it’s as simple as that. For the pharmaceutical company involved it can be a bitter pill to swallow if all the years of hard work and resources have come to nothing. But as Merck found out to its cost, any side effects are best unearthed in the laboratory or during a clinical trial than on the market. And despite what happened to the UK volunteers, it will not put clinical trial regulars off from taking part. Some regulars use trials as a second income, while backpackers see it as a way of funding the next leg of their travels. Peddicord sums up the importance of trials when he says: “In many ways, the controlled clinical trial represents the single greatest advance in the science of medicine in our time. It is a straightforward and rigorous methodology that has, for more than half a century, been the safest and fastest way to find new treatments for the patients that need them. Today there are more biomedical products in development than ever – which is why there are more clinical trials than ever.” ■



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