mean clinical phase times from around 90 to 150 months in the early 1990s.

The magnitude of the increase in trial size numbers does not intuitively imply a quadrupling of costs. But there are also hidden costs, says Kenneth Getz, CEO of CenterWatch. For example, the proportion of clinical studies that are delayed by more than a month has risen from 60% in 1997 to 72% in 2003. As well as adding to the clinical costs, figures from CenterWatch show that every day of prescription drug sales lost due to delays — called 'opportunity costs' — takes an average toll of US $1.3 million, with losses for blockbuster drugs reaching as much as US $4–5 million a day.

A principal reason for delays seems to be patient recruitment. "Half a billion dollars are spent by companies on patient recruitment," says Getz. And 38% of 405 trial sites surveyed by a US Investigative Site Survey in 2003 strongly agreed that slow patient recruitment delayed clinical development. Sites also highlighted contract and budget negotiations, protocol amendments, legal review processes, and institutional review board reviews and approvals as reasons for delays.

Pinning down the reasons for the increase in clinical costs seems to be extremely tricky

Clinical development also incurs other costs. Generally the greatest cost is for enrolling subjects. But hiring personnel from drug companies, drug-production costs, payments to investigators, ethics committees and regulatory authorities, and equipment purchases for laboratories and centres all add to the overall financial burden.

A taskforce called the Pharmaceutical Industry Competitiveness Task Force (PICTF), which was set up by the United Kingdom government to examine the state of the UK pharmaceutical industry, found that one of the most important areas for improvement is in approving and overseeing clinical trials. "These are not headline-grabbing issues, but they are all very important," says Richard Ley, at the Association of the British Pharmaceutical Industry.

Pinning down the reasons for the increase in clinical costs seems to be extremely tricky, which in part results from the scope and complexity of today's clinical trials. A scan of pharmaceutical-related conferences shows a multitude of meetings devoted to improving the efficiency of preclinical technologies, but a relative paucity of those devoted to the analysis of clinical costs. Given that clinical trials are now the most expensive area of drug development, shouldn't getting to the root of the problem be a top priority?

NEWS IN BRIEF

Another Phase III setback for EGFR inhibitor

OSI, Genentech and Roche have announced that their epidermal growth factor receptor (EGFR) inhibitor erlotinib HCl (Tarceva) has shown no evidence of prolonging lifespan when added to standard chemotherapy in lung cancer patients. The news came as no surprise, as it mirrors the failure of another EGFR inhibitor, AstraZeneca's gefitinib (Iressa), in similar circumstances last year. Despite the setback, gefitinib was still approved by the US FDA this year as a single-agent therapy on the basis of Phase II data. Although this creates doubts about whether targeting overexpressed EGFR in tumours is a truly viable strategy, analysts say the true test will come from continuing clinical trials investigating erlotinib HCl as a monotherapy in lung cancer and as a treatment for brain and pancreatic cancer.

Approval ambivalence for Novartis' COX-2 inhibitor

The cyclooxygenase-2 (COX-2) inhibitor lumiracoxib (Prexige) from Novartis is experiencing mixed fortunes. UK regulatory authorities approved the treatment, but a US FDA Advisory Committee has decided to withhold approval recommendation until the company supplies further clinical data. The FDA wants the final report from the ongoing TARGET study — which is comparing lumiracoxib with the nonsteroidal anti-inflammatory drugs (NSAIDs) ibuprofen and naproxen in 13,000 adults with osteoarthritis — and additional, as yet undisclosed, clinical data. The decision is thought to reflect the FDA's increased scrutiny of possible adverse risks associated with COX-2 inhibitors, such as gastrointestinal (bleeding and ulceration) and cardiovascular (heart attacks and stroke) events. Novartis had planned to have a global launch date in 2004, but despite aiming to submit the data as soon as possible, the company does not now anticipate a US launch of lumiracoxib before 2005.

Gene therapy side effects explained

A study published in *Science* has revealed why two out of ten boys in the French arm of a gene therapy trial for X-linked severe combined immunodeficiency (SCID) developed T-cell leukaemia. Trials were halted in France after the two cases were detected, and this led the US FDA to limit gene therapy trials to conditions that are otherwise fatal. In both cases, the retroviral vector carrying a transgene encoding the common γ-chain of the interleukin-2 receptor — the protein that is defective in these patients — was inserted near the promoter of the proto-oncogene *LMO2*. Until the study, the risk from retroviral insertion was presumed to be low as it was thought to be mainly a random event. Consequently, the safety profile of each gene transfer strategy needs to be addressed individually for each disease in relation to its pathophysiology and the functions of the transgene product, say the authors.

Hacein-Bey-Abina, S. *et al. Science* **302**, 415–419 (2003).

Screensavers screen smallpox inhibitors

An initiative that harnessed the power of computers from more than 190 countries has refined its search for a smallpox treatment to 44 molecules. The Smallpox Research Grid Project screened 35 million molecules against eight models of a smallpox enzyme that unwinds the smallpox DNA during replication. This was achieved in less than six months using more than 39,000 years of computer time, in a similar manner to the SETI@home project, which uses screensaver software to analyse radiotelescope data in the search for extraterrestrial life forms. Professor Graham Richards, Chairman of Chemistry at the University of Oxford, and research and industry partners on the project will present the results to the US Department of Defense, who will then pass it on to the US Centers for Disease Control and Prevention.

Alzheimer's drug approved with reservations

Forest Laboratories have announced that the US FDA has approved its *N*-methyl D-aspartate (NMDA) receptor antagonist memantine HCl (Namenda) for moderate-to-severe Alzheimer's disease. The decision was based on the unanimous approval from an FDA advisory committee. But at the same time the committee aired concerns regarding the size of memantine's effect. The committee mentioned in particular the lack of a cognitive measure as a primary end point in one of the trials and a marginally significant result for one of the primary global end points, the Clinician's Interview-Based Impression of Change with caregiver input.

General Electric buys Amersham

One of the world's biggest companies, General Electric (GE), has announced it is buying the UK-based medical imaging and biotech company Amersham for US $9.5 billion to broaden its capabilities in medical technology. GE is a leading manufacturer of positron emission tomography (PET) and magnetic resonance imaging (MRI) scanners. Amersham is a leading manufacturer of contrast drugs used in X-rays and ultrasound, and in MRI and PET. GE said the merger will also help the company enter into personalized medicine. Amersham's laboratory diagnostic expertise will place the new company in a similar position to others, such as Abbott and Roche, which have poured money into molecular diagnostics divisions to develop tests to use alongside medicines.