SOURCE: AUSTRALIA'S CHIEF SCIENTIST

intended to become an emissions-trading scheme in 2015. Australia's 260 largest emitters faced a price of Aus$24 per tonne of carbon dioxide emitted, says Frank Jotzo, a climate-change economist at the Australian National University in Canberra. He says that the price is about three times that set by the current emissions-trading scheme of the European Union.

But the Coalition looks set to act on its promise to replace the system with a 'direct action' plan, which it hopes will meet Australia's target to cut greenhouse-gas emissions by 5% from 2000 levels by 2020. Direct action focuses on government payments to companies that cut their emissions below a specific level, Jotzo says.

Last week, responding to the release of the IPCC's latest report, Hunt said in a statement that the report reinforces the government's "bipartisan support for the science and the targets set for emissions reductions". However, the government's stance on carbon policy and the science-policy vacuum since it came to power have fuelled fears about support for climate-science research.

"There are fears about the funding of climate-change research, particularly on mitigation."

The Coalition released few science policies during its election campaign or when it first came to power, but the scientific community was taken by surprise by Abbott's decision that his "back-to-basics" government would lack a designated minister of science. The government said that the move was aimed at simplifying ministerial and departmental titles. (Critics have pointed out that the incoming government has designated a sports minister.)

PUNCHING ABOVE ITS WEIGHT

Australia's research and development spending is moderate, but its scientific output is among the world's highest per capita.

Responsibility for university research rests with the education ministry, but oversight of government research agencies such as the CSIRO now falls under the purview of the industry minister, Ian Macfarlane.

The industry portfolio will also include natural-resources policy, an area that will consume much of Macfarlane's time, says Kim Carr, former minister for innovation, industry, science and research, and for higher education, who is now the shadow minister for those portfolios.

"I championed the idea of building an innovation portfolio," Carr says. "It was about putting science and research at the centre of the transformation of Australian society. My concern was that if it was in the education area alone, there was a real chance that it would be marginalized. The political attention always goes to the teaching programme, not the research programme." Macfarlane was unavailable for comment.

John Rice, executive director of the Australian Council of Deans of Science, an organization that promotes the development of science in universities, says that the new portfolio configuration poses a "considerable challenge for the government in creating a strong interplay between basic research and innovation".

"I would have thought this government, more than any other, would have recognized the importance of science in supporting the economy," he says.

However, Michael Gallagher, executive director of the Group of Eight, an organization based in Canberra that represents Australia's research-intensive universities, welcomes the move. "There is a narrow culture of short-term, commercially oriented research prevailing in an industry portfolio, whereas Abbott has a broader view of what universities are about," he says.

Christopher Pyne, the education minister, says that the CSIRO and universities will continue to work closely together. "Changing the structure of portfolios will not have an impact on that," he says.

He adds that there will be no cuts to university research, but "some funding will be reprioritized for medical research". He did not respond to a question about the fate of climate-change research. ■

LAW

Uncertainty on trial

Former US drug-company chief appeals conviction for fraud over interpretation of results.

BY EWEN CALLAWAY

Once a pharmaceutical executive and socialite, Scott Harkonen now lives under house arrest and faces professional debarment. His crime: misrepresenting scientific data. But Harkonen is arguing to the US Supreme Court that he did not misrepresent anything.

Federal prosecutors convicted him in 2009 of wire fraud — using false communications to obtain money — for hyping the results of a clinical trial and encouraging the unapproved use of his now-former company's lung-disease drug. Eighteen months later, a judge sentenced him to six months' home confinement and a US$20,000 fine; in March this year, a federal appeals court upheld the conviction.

The United States' highest court will soon decide whether to hear Harkonen's final appeal. His supporters, who include statisticians, clinical researchers and legal scholars, say that his conviction relied on a poor grasp of statistics, and sets a precedent that could criminalize speculation in grant applications and papers.

"You don't want to have on the books a conviction for a practice that many scientists do, and in fact think is critical to medical research," says Steven Goodman, an epidemiologist at Stanford University in California who has filed a brief in support of Harkonen.

The US government sees the case as a warning to those who illegally promote medicines. "Mr Harkonen lied to the public about the results of a clinical trial," the lead investigator said after Harkonen's conviction.

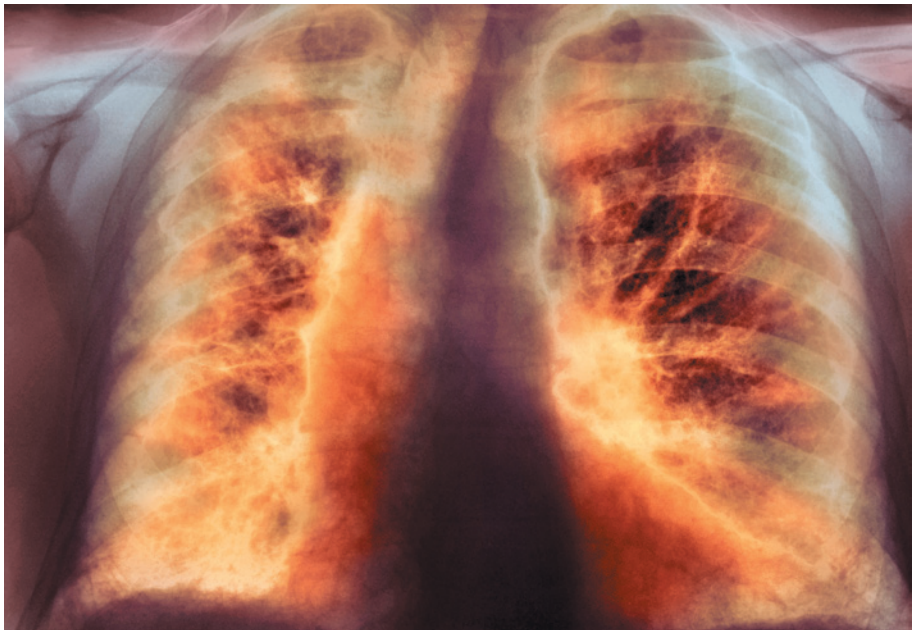
The case centres on a clinical trial sponsored by InterMune, a company based in Brisbane, California, which Harkonen headed from 1998 to 2003. It tested whether a drug called γ-interferon, sold as Actimmune and already approved to treat a rare immune disease, helped people with idiopathic pulmonary fibrosis (IPF), an incurable lung condition.

The results were measured in terms of participants' survival and lung function — primary endpoints, or targets, that had been identified before the trial began. On 16 August 2002, Harkonen and other company executives learned that the 162 participants who had been given γ-interferon had fared no better than ▶

the 168-strong control group. Slightly fewer had died, but the difference was not deemed statistically significant, because the probability that it was not due to the drug was greater than 5%, a widely accepted statistical threshold.

It turned out that when InterMune analysed only the 254 participants who had mild and moderate IPF, the survival difference did meet this important threshold: there were 6 deaths among the 126 people on the drug, compared with 21 among the 128 people on the placebo. But the researchers had not decided to do this selective analysis before the trial, and statisticians consider such 'post hoc' analyses to be less reliable than pre-specified tests.

On 28 August 2002, the company issued a press release, approved by Harkonen, titled 'InterMune announces phase III data demonstrating survival benefit of Actimmune in IPF'. In it, Harkonen said: "We are extremely pleased with these results, which indicate Actimmune may extend the lives of patients." The company noted that the trial had failed to meet its primary endpoint, but did not say that the touted survival benefit had not been pre-specified.



SPL

Lungs affected by idiopathic pulmonary fibrosis become scarred, losing function.

GROWING CRITICISM

The press release quickly prompted concerns. Thomas Fleming, a biostatistician at the University of Washington in Seattle who had chaired the board that monitored the trial's safety, told InterMune that it was misleading, and an official at the US Food and Drug Administration (FDA) told the company that the positive results were inconclusive. The results were later published in the *New England Journal of Medicine* (G. Raghu *et al. N. Engl. J. Med.* **350,** 125–133; 2004).

In 2004, the US Department of Justice launched an investigation into allegations that Harkonen ran a campaign to promote γ-interferon to people with IPF and their doctors — illegal because the FDA had not approved that use of the drug. According to court documents, representatives had received bonuses for boosting sales of γ-interferon, which increased from US$11 million in 2000 to $141 million in 2003, largely owing to off-label prescriptions. Harkonen was charged with wire fraud for distributing "false and misleading" information in the press release, and with false labelling, a charge often used to prosecute off-label drug marketing.

Scott Harkonen says that he did not commit fraud.

The prosecution focused on proving that Harkonen knew that the claims were false and misleading. The jury heard that pre-specified endpoints are the main criteria used to judge the success of a clinical trial, and that post hoc analyses are less trusted. Harkonen was convicted of wire fraud but acquitted of false labelling.

In August this year, Harkonen's lawyers filed an appeal with the Supreme Court, contending — as they did in the original case — that freedom of speech protects the right to express scientific opinions. The US government is due to file a response by early November. If the Supreme Court then decides to take the case, it could hear the appeal in 2014.

Many physicians were encouraged by the results of the clinical trial, even though it did not meet its primary endpoint, says Joseph Zibrak, a pulmonologist at Beth Israel Deaconess Medical Center in Boston, Massachusetts. He used γ-interferon to treat some people with IPF, and says that insurance companies paid for the drug until 2007, when a follow-up trial was ended early because the drug was ineffective. The trial "sort of moved the study of the disease along quite a bit. And it certainly suggested that this was a direction we should continue to pursue," says Zibrak, whom InterMune paid to tell other physicians about his experience using γ-interferon to treat IPF. He has filed briefs in support of Harkonen's previous appeals.

Goodman, who was paid by Harkonen to consult on the case, contends that the government's case is based on faulty reasoning, incorrectly equating an arbitrary threshold of statistical significance with truth. "How high does probability have to be before you're thrown in jail?" he asks. "This would be a lot like throwing weathermen in jail if they predicted a 40% chance of rain, and it rained."

INTERPRETATION IMPLICATIONS

Gordon Guyatt, a researcher at McMaster University in Hamilton, Canada, who is not involved in the case, agrees that a clinical trial failing to meet its primary endpoint does not mean that the drug does not work. But he thinks that Harkonen skewed the findings. "This guy gave a very unbalanced presentation; whether it is sufficiently unbalanced that you should send him to jail, I don't know," he says.

Patricia Zettler, a former FDA attorney who was not involved in the case and is now a fellow at Stanford Law School's Center for Law and Biosciences, doubts that the case will make a difference to most scientists. She adds that the Supreme Court is unlikely to hear a fraud case, for which free speech is not usually protected.

Harkonen faces professional sanctions: the US government is seeking to prevent him working for companies that receive federal health funding or that develop drugs that require FDA review. In 2010, he stepped down as chief executive of Comentis, a San Francisco biotechnology company. But Harkonen tells *Nature* that he is most worried about the implications of his conviction for research. "I'm committed to going forward until the courts get the science straightened out," he says. ■