

Former Novartis employee arrested over valsartan data

Novartis is facing a new scandal after an ex-employee was arrested last week following allegations of scientific misconduct. Justin McCurry reports from Tokyo.

A former employee of Novartis Pharma KK, the Japanese subsidiary of Novartis, has been arrested (June 11) on suspicion of falsifying clinical data to overstate the benefits of the Swiss drug manufacturer's hypertension drug valsartan.

63-year-old Nobuo Shirahashi is accused of passing on falsified data to researchers that suggested that the drug, a popular treatment for high blood pressure in Japan, where it is marketed as Diovan, had secondary medical benefits. The research was later used in advertising campaigns for Diovan in Japan.

Prosecutors raided the company's Tokyo headquarters after a university involved in the studies said the results seemed to have been manipulated to attribute qualities to Diovan that it did not possess, such as preventing stroke and angina.

Shirahashi, the former director of Novartis Pharma's scientific affairs department, faces up to 2 years in prison or a maximum fine of JPY 2 million if found guilty of violating Japan's pharmaceutical laws. According to Kyodo news agency, Shirahashi denies allegations that he provided false stroke incidence and other data to researchers at the Kyoto Prefectural University of Medicine, prompting them to endorse Diovan in a paper published in 2011.

Novartis Pharma said it would cooperate with the investigation. "Regarding the arrest of our former employee, we take this seriously", it said in a statement. "We will continue to cooperate completely with the investigating authorities, and we again apologise deeply for the concern and difficulties this has caused to the public."

While a Novartis Pharma employee, Shirahashi had been responsible for analysing data from clinical trials

comparing Diovan with other drug treatments for high blood pressure done by the Kyoto medical school and four other universities from 2002–10, according to Japanese media reports.

Based on data for 3000 patients provided by Shirahashi, researchers at Kyoto concluded that Diovan was the most effective of all the drugs analysed at preventing stroke and angina. Shirahashi, who left the company in May, 2013, allegedly altered charts

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comparing the frequency of stroke in trial participants who were given Diovan and other hypertension drugs, before submitting the falsified data to the Kyoto researchers. According to the *Mainichi* newspaper, the data was sent to Kyoto University between November, 2010, and September, 2011.

Novartis Pharma is unlikely to escape scrutiny over its part in the alleged malpractice, with prosecutors expected to seek legal action against the firm for failing to prevent misconduct by its employees.

Diovan has enjoyed impressive sales in Japan since it was made available there in 2000. Sales were worth more than JPY 100 billion in 2012, while cumulative sales have reached JPY 1.2 trillion.

Novartis Pharma is still reeling from allegations that it had not disclosed all of the possible side-effects of its leukaemia treatment nilotinib, marketed as Tasigna. The company's troubles deepened when a third-party commission it had set up found that

employees might have broken Japan's strict privacy laws by illegally acquiring information about patients involved in clinical trials for Tasigna.

Novartis Pharma KK was initially suspected of failing to report 33 cases of side-effects involving Tasigna, including ten that were deemed severe, to Japan's health and welfare ministry following a clinical study led by Tokyo University, according to Kyodo news sources. That revelation prompted an investigation into alleged violation of the pharmaceutical affairs law. The firm has since acknowledged that at least 10 000 cases involving ten different medicines might have been involved in a safety cover-up dating as far back as 2002.

In April, Novartis Pharma KK responded to the Diovan and Tasigna revelations by replacing its president and two other senior executives. It is also reviewing all doctor-led studies in which the firm has been involved in since 2011. Several other employees implicated in professional misconduct have been sacked, while funding for collaborative research with universities and other research bodies has been suspended.

Before Shirahashi's arrest, the president of Novartis, David Epstein, said he was "surprised" by evidence that the firm's Japanese unit had manipulated data and under-reported side-effects. But he declined to say if the firm would return profits made from use of possibly manipulated data for Diovan.

Two studies on valsartan were retracted last year. The Kyoto Heart Study published in the *European Heart Journal* in 2009 was retracted in February, 2013. The Jikei Heart Study published in *The Lancet* in 2007 was retracted in September, 2013.

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Dr P. Manazil/Science Photo Library