



France Warns US Buyer of Sanofi Division of Penalties For Shifting Production Abroad



The French government has warned a US private equity firm buying the consumer healthcare arm of the drugmaker Sanofi that it faces penalties of more than €100m if it does not keep production and jobs in France.

Sanofi is splitting off Opella, which makes the paracetamol brand Doliprane, the laxative Dulcolax and other over-the-counter medicines and vitamins. However, news of talks with the New York-based Clayton, Dubilier & Rice on 11 October prompted fears about French jobs and the loss of control to a foreign company.

On Monday, Sanofi announced that it had entered exclusive negotiations with CD&R for the sale of a 50% stake in the consumer business, valuing it at €16bn. However, France's state-owned investment bank, Bpifrance, will also take a 2% stake and a seat on Opella's board.

France's economy minister, Antoine Armand, said that under a trilateral agreement thrashed out with Sanofi and CD&R over the weekend, Opella's new American owners will have to keep key factories, research, management and its 1,700 workforce in France. CD&R pledged to invest €70m in France over the next five years.

"To ensure that these guarantees are respected with the utmost rigour and firmness, [there will be] firm, immediate and far-reaching sanctions," Armand said as he presented the deal alongside the industry minister, Marc Ferracci.

Opella would have to pay a €40m penalty if it were to stop production in its factories in Lisieux and Compiègne in northern France, which produce popular medicines such as Doliprane and drugs to treat allergy and digestion problems, over the next five years, and there is the potential to extend this requirement.

Workers at both factories have been on strike to protest against the deal since the news broke. Under the deal, Opella will have to pay a €100,000 fine for every economic-related layoff. The agreement also requires Opella to source the active ingredient for the production of paracetamol from the French supplier Seqens under a long-term contract. Opella will have to pay €100m penalty if it breaks that promise.

Paris-listed Sanofi said it would retain a significant stake in the division but would focus on producing innovative medicines and vaccines. (Source: The Guardian)

Covid-19 May Increase The Risk Of Heart Attacks, Strokes And Deaths For Three Years After an Infection, Study Suggests

Covid-19 could be a powerful risk factor for heart attacks and strokes for as long as three years after an infection, a large new study suggests. The study was published Wednesday in the medical journal *Atherosclerosis, Thrombosis, and Vascular Biology*. It relied on medical records from roughly a quarter of a million people who were enrolled in a large database called the UK Biobank.

Within this dataset, researchers identified more than 11,000 people who had a positive lab test for Covid-19 documented in their medical records in 2020; nearly 3,000 of them had been hospitalized for their infections. They compared these groups with more than 222,000 others in the same database who didn't have a history of Covid-19 over the same time frame. People who caught Covid in 2020, before there were vaccines to blunt the infection, had twice the risk of a major cardiac event like a heart attack or stroke or death for almost three years after their illness, compared with the people who didn't test positive, the study found. If a person had been hospitalized for their infection, pointing to a more severe case, the risk of a major heart event in was even greater – more than three times higher – than for people without Covid in their medical records. What's more, for people who needed to be hospitalized, Covid appeared to be as potent a risk factor for future heart attacks and strokes as diabetes or peripheral artery disease, or PAD. One study estimated that more than 3.5 million Americans were hospitalized for Covid between May 2020 and April 2021.

A finding unique to Covid-19

The elevated heart risks from infection did not appear to diminish over time, the study found. "There's no sign of attenuation of that risk," said study author Dr. Stanley Hazen, who chairs the department of Cardiovascular & Metabolic Sciences at the Cleveland Clinic. "That's actually one of the more interesting, I think, surprising findings." That finding is striking and seems to be unique to Covid-19, said Dr. Patricia Best, a cardiologist at the Mayo Clinic in Rochester, Minnesota, who was not involved in the research. "We have known for some time that infections raise your risk of having a heart attack, so that if you have influenza, if you get any kind of infection ... whether it's bacterial or viral, that increases your risk of having a heart attack," Best said. "But it generally goes away pretty quickly after your infection. 'This is just such a large effect, and I think it's just because of how different Covid is than some of the other infections,'" she said.

The researchers involved in the study say they don't know exactly why Covid has such apparently long-lasting effects on the cardiovascular system. Earlier studies have shown that the coronavirus can infect the cells that line the walls of blood vessels. The virus has also been found in sticky plaques that form in arteries that can rupture and cause heart attacks and strokes. "There might just be something that Covid does to the artery walls and the vascular system that is sustained damage and just continues to manifest over time," said study author Dr. Hooman Allayee, a professor of biochemistry and molecular genetics at the Keck School of Medicine at the University of Southern California. Their working theory, Allayee said, is that Covid may be destabilizing plaques that are building within the walls of arteries and may make them more prone to rupturing and causing a clot. Allayee and his graduate student James Hilser took a closer look to see how Covid might be causing this long-term trouble in the body. They looked to see whether people with known genetic risk factors for heart disease, or gene changes linked to being susceptible to Covid infection, were more likely than others to have a heart attack or stroke or to die after being hospitalized for Covid. But they weren't. What did show up, the researchers say, was a distinction by blood type. Researchers have known that people with certain non-O blood types – A, B or AB – are at higher risk of cardiovascular diseases.

Blood type also appears to play a role in how likely a person is to get Covid. People with O-type blood seem to be a bit protected there, too. In the new study, people with O-type blood who were hospitalized for Covid didn't have quite as high of a risk of heart attack or stroke as those with A, B or AB blood types. But that doesn't mean they were in the clear, Hazen said: They were still at higher risk of heart attacks and strokes, but their blood type was just another variable to consider. The researchers believe that the gene that codes for blood type may be playing a role in the increased risk in heart attacks and strokes after Covid, but they aren't sure exactly how.

There was some hopeful news in the study, too. People who were hospitalized for Covid but who were also taking low-dose aspirin had no increase in the likelihood of a subsequent heart attack or stroke. That means the risk can be mitigated, Hazen said. "Cardiac disease and cardiovascular events are still the number one killer around the world," he said. When he sees patients, Hazen said, he now makes sure to ask about their Covid history. "If you've had Covid, we have to be especially attentive to making sure that we're doing everything possible to lower your cardiovascular risk," Hazen said. That includes controlling blood pressure and cholesterol and perhaps taking a daily aspirin.

The study didn't look at the effects of Covid-19 vaccination on a person's cardiovascular risk, but Hazen suspects that it would be protective, because vaccines usually keep Covid infections from becoming severe. The study also didn't dig into whether repeated Covid infections might be tied to even greater health risks, as some research has found. Still, Hazen said, anyone who was hospitalized for Covid – whether vaccinated or not – should be attentive to their heart risks. (Source: CNN)

India's Pharma Industry Reduced US Healthcare Costs By \$219 Billion in 2022



India's global pharmaceutical position has contributed to substantial reductions in healthcare costs in the US. The country is also producing nearly half of the world's vaccines.

Indian-made medicines have helped the US healthcare system save \$219 billion in 2022. India manufactures nearly half the world's vaccines, over 4 billion doses in 2023.

40 million vaccine doses are being manufactured for cancer prevention efforts.

India is the third-largest producer and a major supplier of generic medicines in the world. At the India Leader Summit 2024, Union

Health Secretary Punya Salila Srivastava highlighted that India's global pharmaceutical position has led to massive savings for healthcare systems worldwide, particularly in the US.

"India's pharmaceutical industry stands out with the largest number of US FDA-approved pharmaceutical plants outside the US, accounting for 25% of all such facilities. Indian-made medicines have helped the US healthcare system save \$219 billion in 2022 and \$1.3 trillion between 2013 and 2022," she mentioned. During the US-India Strategic Partnership Forum, the union secretary said India manufactures nearly half the world's vaccines. "Out of the 8 billion vaccine doses produced globally last year, India manufactured 4 billion doses," she added, mentioning that India is known as the "pharmacy of the world."

India has also implemented reforms in medical education, replacing outdated regulations with the National Medical Commission Act. This has resulted in a rise in the number of medical and nursing colleges, bridging gaps in the availability of healthcare professionals.

The health secretary noted that India is preparing a health workforce that will not only meet domestic needs but also contribute globally.

"Out-of-pocket expenditure has dropped by 25% points as a share of total health expenditure between 2013-14 and 2021-22," she stated.

She also underscored the strong health partnership between India and the US, particularly in areas such as pandemic preparedness, disease surveillance, and antimicrobial resistance.

The role of collaboration between the National Centre for Disease Control (NCDC) and the US Centers for Disease Control and Prevention (CDC) was also highlighted with programs such as the Field Epidemiology Training Programs (FETP).

"Over 200 Epidemic Intelligence Services (EIS) officers have been trained, with 50 more currently in training," she said.

In addition, India and the US have initiated a strategic framework to optimise the biopharmaceutical supply chain through the Bio-5 alliance. In 2023, the two nations committed to advancing cancer research, leading to the launch of the US-India Cancer Moonshot Dialogue, which focusses on biomedical cooperation, particularly in cervical cancer research.

This initiative includes collaborations with Indian institutions such as AIIMS and Tata Memorial Hospital and has evolved into the Quad Cancer Moonshot Initiative.

As part of this, a grant of \$7.5 million has been allocated for cancer diagnostics in the Indo-Pacific region, and India is contributing 40 million vaccine doses to support cancer prevention efforts under the GAVI and Quad programs.

Initiatives like the Indo-US Health Dialogue have already made strides in disease surveillance and pandemic preparedness.

The health secretary expressed optimism that the two countries will continue to strengthen global health security by advancing research, technology transfer, and capacity building through public-private partnerships and joint vaccine initiatives. (Source: India Today)

Despite Valuations Surge, Pharma Firms Still Have Headroom to Grow

In the last 10 years despite being integral to the Indian economy, the market capitalisation of none of the pharma companies ever breached the ₹1-lakh-crore mark, barring Sun Pharma. For a brief period in FY20-21, even Sun Pharma was valued below ₹1 lakh crore. But as of today, seven companies have breached the psychological mark and Sun Pharma set a new benchmark with a valuation of ₹4.5 lakh crore.

Divi's, Cipla, Torrent Pharma, Dr. Reddy's, Zydus Lifescience and Lupin have evidently gained from improved valuations ascribed to the sector apart from operational growth, with Nifty Pharma trading at 30 times the one-year forward EPS now compared to 23 times in 2014. But viewed from a balance-sheet perspective, the sector holds more promise despite the rich valuations. Our analysis of 48 pharma companies with available data revealed strong balance-sheets. While the asset turnover has shrunk impacting profitability, if companies leverage this wide asset base, further growth can be charted from here.

Asset rise tops revenue

The companies reported a gross block growth of 13 per cent CAGR in the last 10 years (FY14-24) compared to 10 per cent revenue growth. This has resulted in companies reporting a lower utilisation of assets. The asset turnover ratio has shrunk from 1.5 times in FY15 to 1.1 times now. Among the top five, Torrent Pharma saw the sharpest decline (1.9 to 0.8 times) as the company acquired Curatio (₹2,000 crore) and other assets in the period.

In varying degrees, the sector followed the same path adding assets organically or inorganically, but the utilisation levels are below peaks in the recent period. The faster asset addition is despite a persistent trend of CMOs (contract manufacturing outsourcing) shouldering a large part of the demand sourced from these companies. The gross block addition also encompasses R&D labs or plants for backward integration. While not contributing directly to topline, the benefit should flow through on optimal utilisation. It is pertinent to note that despite the asset growth, pharma continues to be a low debt sector and the overall leverage has declined. The sector net debt to EBITDA has come down from 0.6 times to 0.3 times in FY14-24. The sector did witness an increase to 1.4 times by FY19 before the reversal started, especially in FY24, when the net debt declined 37 per cent.

Room for more profitability

That said, lower utilisation of assets has impacted profitability. The EBITDA and PAT margin for the sector have declined from 26/16 per cent to 24/12 per cent in FY14-24. The impact of the recovery in the US segment (which earlier faced high price erosion) can be seen in the FY24 margins being better than FY23. But the full recovery could have been held back by lower asset utilisation resulting in inability to absorb the higher overheads. The pharma rally over the past year has been driven by favourable market dynamics in India and the US. Improved asset utilisation could boost growth further. Though valuations seem expensive, this may benefit pharma players. Investors should watch asset utilisation trends closely (Source: Business Line)

Diabetes Drug Metformin Safe For Men Who May Become Fathers, Study Finds



Men can take the widely prescribed diabetes drug metformin without fear of causing birth defects in their children, according to results of a large study published on Wednesday. Tracking more than 3 million pregnancies in Norway and Taiwan, researchers found no association between birth defects and use of metformin by fathers during the three months before conception, which is the period of sperm development. Metformin, a relatively inexpensive generic medicine, is typically the first drug prescribed for Type 2 diabetes, by far the more prevalent form of the disease. A 2022 study from Denmark had found that metformin was associated with a 1.4 times greater risk of birth defects in

boys whose fathers were taking the drug. Studies conducted since have not confirmed that association. In June, a pair of studies published in *Annals of Internal Medicine* suggested that neither maternal nor paternal metformin use increases the risk of congenital malformations.

The use of data from two different populations in Norway and Taiwan strengthens the new study's results, Dr. Allan Pacey, an expert in male reproductive health issues at the University of Manchester in the UK, said in a statement. The new finding that no link exists between a father's metformin use and birth defects "makes sense because there was never any plausible biological mechanism which might have led us to this conclusion," Pacey said. "I think the reasons that this new paper finds no link, compared to the 2022 paper which did, is simply down to data quality," added Pacey, who was not involved in either study. "Both analyses were very well conducted, but in this paper... the authors were able to take into account many more confounding factors," he added. (Source: Reuters)