



Gene therapy risky business for patients

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seattlepi.com

August 16th, 2007

TARGETED GENETICS Corp. is caught in the middle of a brewing storm: Jolee Mohr, a vibrant 36-year-old mother, recently died while participating in a gene therapy clinical trial for arthritis run by the Seattle-based biotech firm.

Since the '80s, gene therapy -- an experimental procedure that attempts to treat a disease by replacing damaged genes with new ones -- has been widely touted as modern medicine's next marvel. Sad to say, it has been implicated in an assortment of "serious adverse events" and deaths; no gene therapy treatment has ever been deemed safe or effective enough to receive FDA approval.

Although the FDA has not confirmed Mohr's cause of death, all available evidence points to the engineered virus given to her during the clinical trial. Until now, the most well known gene therapy death was Jesse Gelsinger's, an 18-year-old with a rare metabolic disorder.

Gelsinger died when his immune system responded poorly to the treatment -- symptoms similar to Mohr's. Also like Mohr, Gelsinger died when the risky gene therapy procedure was used to treat a non-life-threatening condition that could have been managed with safer alternatives.

What's going on here? Why is an unproven procedure linked to multiple deaths being tested on people with non-fatal illnesses?

Those tragedies reflect one of the more troubling regulatory failures in the U.S. health care system: the inability to develop sensible and enforceable rules to oversee a

growing biotech industry that is using humans to test what it hopes will become the next big moneymaker -- all without having much of a clue as to gene therapy's long- or short-term impacts.

When a federal committee charged with reviewing gene therapy trials evaluated Targeted Genetics' arthritis study in 2003, members openly questioned its justification, as it involved patients who were not very ill and evidence from animal studies didn't seem all that promising. They also worried it could trigger dangerous immune responses and questioned the informed consent documents' clarity. But as they have no binding authority or enforcement powers, Targeted Genetics was free to continue as it saw fit.

But this isn't simply about regulatory failure. It's also about how profit motives embedded in the clinical trial process can undermine patient safety. Pharmaceuticals had the fifth-most profitable return on revenues of any industry in 2006; the top five drug companies took home close to \$30 billion in profits. Such companies as Targeted Genetics hope gene therapy and other biotech products will help them tap into and expand those markets. To be sure, Targeted Genetics CEO H. Stewart Parker told the P-I in 2005 that arthritis treatment could be "a \$7 billion market ... by 2011" and that the gene therapy used in the clinical trial that may have led to Mohr's death might help the company capture "15 percent to 40 percent of that opportunity."

Time is money; in the rush to get products to market, patient safety can inadvertently take a backseat. And the fact that Targeted Genetics doesn't currently have any products on the market suggests that it has a significant financial incentive to stop hem-

orrhaging cash -- financial reports indicate it has lost \$8 million this year alone -- and do everything possible to quickly get its products out of the clinical trial phase.

Other questionable financial dealings might also influence decisions that could affect trial participants' overall safety. For example, Targeted Genetics paid Mohr's arthritis doctor for recruiting her and other patients to the clinical trial. That raises questions about whether Mohr's trust in her personal physician obscured the risks associated with gene therapy and the fact that she was unlikely to benefit from the procedure.

It's also important to note that the institutional review board charged with ensuring that the trials were conducted ethically is a for-profit enterprise also on Targeted Genetics' payroll. When a review board is being paid by the company that it is supposed to oversee, incentives often lean the wrong way: toward helping industry profit and away from patient safety.

Such practices are common in today's clinical trials, and they put people's lives in danger. With so much money in play and so little enforceable oversight, corners may be cut more often than we'd like to think.

The FDA's reaction to this tragedy will have a tremendous impact on gene therapy's future and the public's trust in government's ability to protect the safety of participants in medical research. Any company that puts profit before patient safety must be held to account.

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