Study Case 1. Gelsinger, OTC and Risks of Gene Therapy

Ornithine transcarbamylase (OTC) deficiency is a genetic disease which prevents the body from breaking down ammonia (a metabolic waste product). In OTC patients, the excessive build-up of ammonia often causes death soon after birth, unless the patient's diet is immediately adjusted and monitored throughout their entire life.

A 17-year-old boy named Jesse Gelsinger with OTC deficiency was fairly well controlled on a strict non-protein diet. In 1999, Jesse volunteered for an experimental gene therapy, at the University of Pennsylvania, designed to test a possible treatment for OTC in which an adenovirus vector carrying a normal OTC gene was injected into his liver. Prior to entering the study, Jesse and his family were informed that other subjects had received adenovirus infusions without serious complications. Following the infusion, Jesse suffered an unusual reaction triggered by the injection of the adenovirus vector, which in turn triggered a fatal hyperactivation of his immune system reaction. On September 17, 1999, four days after the injection, Jesse Gelsinger died.

Following Jesse Gelsinger's tragic death, investigations by a number of different agencies and scientific experts revealed new information and insights about prior research and clinical experiences which had great relevance to current and future gene therapy research and treatment.

Research investigators gave considerable thought to the selection of subjects for these gene therapies: healthy, adult volunteers who had OTC or babies born with OTC whose parents consented. A concern was raised as to whether parents with very sick newborns could really understand that gene therapy experiments were very risky and probably would not help their baby. Ultimately, the research investigators chose adults, who were thought more likely to have better comprehension.

Although initially it was thought that the adenovirus vector system was relatively safe and that Jesse’s deadly reaction was random and unforeseeable, the investigations turned up some 700 instances of adverse events among gene therapy subjects (human and animal). Although most of these events had been reported to the FDA, the agency had neglected to set up a formal tracking and information sharing system because of pressure from the gene therapy industry. Consequently, these previous problems had not been communicated adequately to stakeholders in gene therapy community, including volunteer subjects, families, and other members of the research community. Jesse’s family said that they were never adequately informed of these past events, and that when Jesse decided to volunteer, he thought the risks were lower than they actually were.

The lead scientist, Dr. James Wilson, held more than 20 patents related to gene therapy, and also held 30% of the stock in a small startup company, Genovo, which was sponsoring the research and clinical testing. In addition, the University of Pennsylvania also held some of the stock in Genovo. Investigators concluded that Gelsinger had not been fully apprised of the financial interests of the research institute and investigators. If the adenovirus vector being used in the OTC gene therapy trial worked correctly and was successful, the investigators and the affiliated institutions stood to earn a large amount of money, and to benefit in many other respects, such as using it to treat people or selling it to other researchers and physicians.

Adapted with modifications from http://highschoolbioethics.med.nyu.edu/briefs/jesse-gelsinger
Questions for Discussion

Describe how their financial stakes in the OTC gene therapy might have influenced some scientific and/or clinical decisions made by Dr. Wilson and associates as he continued with his investigations.

Do you think a researcher can make sound decisions about an experiment when they have a stake in the outcome of those experiments?

Do you think researchers can make ethically sound decisions about clinical investigations when they have financial or intellectual stakes in the outcome of those experiments?

Do you think there are any conflicts of interest in the deliberations about choice of research subjects? Would you make the same decision?

Describe how the various financial arrangements described in this case constituted or led to conflicts of interest.
Case Study 5: Who Owns Research Data?

Jessica Banks, a Ph.D. student working with Professor Brian Hayward, a sociologist studying urban sprawl, has recently defended her dissertation and is now ready to file it and leave for her new job. During her second year, when starting research with Hayward, Banks divided her time among three projects. Then, in her third year, after consultation with Hayward, she decided to continue and expand upon one of the three lines of investigation for her dissertation research. This was also the project most closely related to Hayward's grant at the time. Later, Banks's experimental plan and early results were included in Hayward's grant renewal. The other two promising lines of research were left incomplete.

Shortly before leaving for her job, Banks comes to Hayward's office to make copies of research data stored only on Hayward's computer using special software, which she also plans to copy. Although her new faculty position will place a heavy emphasis on teaching, she is looking forward to continuing to do some research as well. In particular, she is eager to pick up where she left off with the two incomplete projects she worked on earlier. Hayward comes in as Banks is downloading her material, and asks her what she is doing. She tells him, and he then says to her that she cannot take the data. "They belong to me," he says. Banks is confused. "But I did the work, and I wanted to follow up on it. I can't do that without the data." Hayward is adamant. "I'm sorry, but you should understand this. Our research project was a joint enterprise, and all the work you did was funded by money I brought in via grants. The data do not belong to you or to me; they actually belong to the university, and the work will be continued with other students. I've already talked to one of the new students about working on those projects this fall." Banks, seeing her plans fall apart around her, protests, but Hayward is implacable.

After a few minutes, she stalks away. Later that afternoon, Banks gets together with her classmate Paul Larson, and she tells him about her run-in with Hayward. "Look," Larson says. "Hayward has no right to deny you access to data. You did the work that generated all the data." "I know!" Banks says. "But Hayward wouldn't listen to that argument when I made it." "Here's my suggestion," Larson says after some reflection. "Just stop by his office and copy it sometime during the weekend. I happen to know Hayward will be out of town, so he'll never know. That's the fair thing to do." Banks seems uncertain, but she says she'll think about Larson's suggestion and decide before the weekend.

Case Study 5: Who Owns Research Data?

1: Who owns research data? Do you think this policy is fair?

2: How could this problem of access to the research notebooks and manuals have been avoided?

3: Under what conditions should copying of data been done?

4: Are the policies of data ownership clearly defined in research projects in which you are engaged?