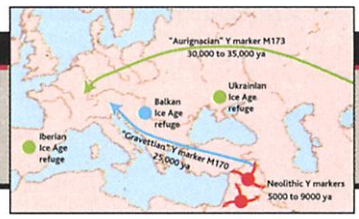

CLINICAL TRIALS

Company, Researchers Battle Over Data Access

A dispute between university-based researchers and the corporation that funded their study is threatening to erupt into a $7 million to $10 million legal battle. Last week, the researchers reported that a large clinical trial of an immune system booster to treat HIV-infected people found that the drug isn't effective in slowing progression to AIDS or reducing mortality. The company that developed the drug tried to block publication of the study unless the researchers included the company's analysis of a subset of the data that suggests the drug might help some people. The researchers refused.

This nasty dispute has again raised the issue of who controls the data when corporate and academic interests conflict. "This is probably the unusual case, where investigators and the journal are standing up to the supporting companies," says science policy analyst Sheldon Krimsky of Tufts University in Medford, Massachusetts. "More typically, you find investigators willing to compromise to avoid legal action or loss of funding for future projects."

The study is believed to be the largest randomized clinical trial among HIV-infected persons in the last decade. The 3-year, double-blind study of 2527 otherwise healthy HIV-positive people at 77 U.S. sites tested a drug called Remune, developed by Immune Response Corp. of Carlsbad, California. Immune Response and the University of California, San Francisco (UCSF), Center for AIDS Research funded the research.

The trial ended in May 1999 when an independent safety monitoring board decided that the drug showed no clinical benefit and was unlikely to do so. That's when trouble started brewing, says AIDS researcher James Kahn of UCSF, the study's national principal investigator. In the news release announcing the trial's early end, Immune Response claimed that an analysis of a subset of people who underwent more frequent blood tests indicates that Remune reduced the amount of HIV in their blood—the "viral load." This effect, the company noted, would be the basis of its application to the U.S. Food and Drug Administration for marketing approval for the immunogen. (Another trial, focusing on the drug's effect on viral load, began in September 1999.) Kahn and the study leadership team conducted a preliminary analysis of a larger sample, which they presented at a fall meeting in San Francisco. Remune, they concluded, had no apparent clinical effect and no discernible effect on viral load.

In January, the disagreement about how to summarize the virologic effects led the company to propose that Kahn, biostatistician Stephen Lagakos of the Harvard School of Public Health in Boston, and two other researchers could have access to the complete data set—which the company controlled—if they agreed to written company approval of "the content, analysis, results and discussion" before publication, according to a memo from the company to Kahn and his team. The memo also asked for prior approval of any further analysis and to limit the researchers' access to the data to 1 year. "We were flabbergasted that they would put new conditions on getting the data, and we objected strenuously," Kahn says.

Publish and be damned. UCSF's Kahn decided to publish paper over company's objections.

The researchers didn't accept the terms. Instead, they used the data submitted to the safety board, which they say is 95% of the results on clinical progression. This summer, they sent both a draft and then the final manuscript to Immune Response for review to ensure that it contains no proprietary information, as required by their contract. The researchers incorporated some revisions, but refused to add a figure illustrating the company's analysis of the subset data.

Ronald Moss, Immune Response's vice president for medical and scientific affairs, says that "despite the failure to show significant differences in clinical endpoints, [the company's subset analysis] gave us valuable insight into the potential effects of Remune on viral load and T cell help. … The Remune group is favored at weeks 36, 48, 60, 84, 96, and 120 … we felt it was extremely important to have a section in the paper describing and discussing the results." Lagakos counters, however, that he also analyzed the data for the subset, and "there were no significant differences using the analytical methods specified in the protocol." Kahn adds: "Immune Response used a statistical test that was inappropriate for the data. The company thinks 'data dredging' makes sense. There are no differences at certain interim time points, and there are differences at others. One cannot pick and choose data points to suit one's needs."

When it was clear that they would not reach agreement, Immune Response invoked a contract clause asking for legally binding arbitration, seeking damages of $7 million to $10 million. The company claims that the research agreement gives the researchers access only to data generated by the UCSF site, and that data from other sites are confidential. UC has filed a counterclaim asking for the complete data set and maintaining the right to publish further analyses. "In every one of three key documents—the research agreement, the protocol, and the site agreement—there is very clear language that the study team will publish the results of the study and that they have the right to do that," says UC counsel Christopher Patti.

The researchers submitted their manuscript in September to the *Journal of the American Medical Association*, which quickly published the paper in the 1 November issue along with a cluster of articles and a commentary that address academic conflicts of interest with industry research sponsors.

The controversy has sparked curiosity about the company's version of the subset analysis. Alexandra Levine of the University of Southern California in Los Angeles says that the researchers should have included the company's data. "Why not give the reading audience full access to the data?" she says. "If the authors are presenting data fairly, then present all of it."

Moss says the full story will be out soon; other investigators involved in the clinical trial will publish another analysis, with the disputed figure, possibly in January.

–CAROL CRUZAN MORTON

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