

Hopkins Can Resume Studies -- Within Limits

Long Delays Expected In Many Human Tests

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Johns Hopkins University can resume federally funded medical research involving human subjects on a limited basis following an intense weekend during which school and government officials agreed on a plan to solve "systemic problems" in how projects were being approved and monitored.

The decision by the federal Office for Human Research Protections comes with numerous restrictions that may delay more than three-quarters of 2,800 clinical trials for weeks, if not longer.

The university will have to scrutinize the approvals given those thousands of trials and determine whether they followed a legitimate discussion and vote. If not -- and agency spokesman Bill Hall predicted that a large number probably did not -- Hopkins's institutional review boards will have to reassess each -- one by one.

"It's probably going to take a while," he said. "It's not an easy task."

Since the federal agency ordered Hopkins last Thursday to stop all federally supported trials -- broad action triggered in part by the death last month of a healthy young woman in an asthma study -- researchers at the university's medical and nursing schools, hospitals and affiliated centers have been inundated with calls and notes from patients worried about what was happening and what it might mean for their treatment.

Those researchers can continue to provide care and medication as long as they believe it is in the "best interests" of their subjects, such as providing life-sustaining or palliative drugs, but a Hopkins statement to faculty and staff specifies that separate justification must be provided.

Enrollment of new subjects remains suspended "except in extraordinary cases approved in advance" by the Office for Human Research Protections, according to a letter sent Sunday by Michael Carome, director of the agency's compliance oversight division.

While the agency's approval of Hopkins's plan to correct flaws in its research review process was a major first step, university spokesman Gary Stevenson conceded yesterday that "there is a mountain of work that remains to be done under any scenario."

The only studies that immediately can continue are those that pose no more than minimal risk to participants because they involve nothing more invasive than blood or urine samples, ultrasound tests or psychological survey questions.

Those are relatively few in number, however. Of 2,800 projects that were affected last week, 2,050 remain suspended as officials read over minutes of review board meetings and try to determine whether their initial reviews followed regulations.

In cases where officials determine that all steps were followed appropriately, that research then can be reinstated.

But a vast number of studies will remain on hold. Neurologist David Cornblath, who leads an institutional review board at Hopkins's East Baltimore campus, expects that it might take until Thanksgiving "to get all those up and running again." Hopkins does a prodigious amount of medical research, supported by \$300 million in federal funds, more than any other school in the country.

What lies ahead is "staggering," Cornblath said yesterday evening, and he and other officials are trying to determine how to triage the load. Studies involving oncology research, as well as AIDS, probably will be given the highest priority as the university's three review boards begin their work. One or more boards will be meeting virtually every day for a while, he said.

"If you happen to be a poor investigator who wishes to do a new protocol, forget it," Cornblath warned. "Because you're going to go to the bottom of the list."

The federal action last week came three days after the university's medical leaders acknowledged multiple flaws in the process by which an asthma trial had been constructed and approved.

Ellen Roche, 24, was one of nine volunteers in that trial, which was looking at how and why healthy lungs counteract the airway constriction that can cripple or kill people with asthma. The project involved inhaling hexamethonium and did not alert participants that the chemical can carry significant risk, yet Roche became ill almost immediately. She died of acute respiratory distress syndrome several weeks later.

When federal investigators visited Hopkins last week to review research documents and conduct interviews, they found "systemic problems throughout the institution" that they decided required an immediate and severe response, Hall said yesterday.

In some cases, Hopkins acknowledges, minutes of particular review board meetings were not typed and recorded. In others, research proposals may have been voted on simultaneously or board meetings not properly convened. The federal agency also faulted the university on numerous other points, including situations in which board members participated in reviews in which they had a conflicting interest.

Carome's latest letter to university officials noted "the extraordinary efforts that your faculty and staff have made to develop [this] corrective action plan and to begin the initial steps to improve your system for protecting human subjects."

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