nature medicine
VOLUME 5 • NUMBER 6 • JUNE 1999

A higher standard for human research

Duke University is a giant in the arena of biomedical research. Its School of Medicine is in the top ten for grant support from the US National Institutes of Health (NIH), ahead of such luminaries as Baylor, Harvard and UCLA. It boasts major research initiatives in every area of biomedical research and a history of discoveries that ranks it amongst the best biomedical research institutions worldwide. It was all the more surprising, therefore, to see it added to the small but growing list of institutions to have their NIH license to conduct human research suspended. Fortunately, for all concerned, the suspension lasted no more than a few days. Nonetheless, the biomedical research community should take note that a documented safe and ethical approach to human research is a rule that cannot be bent.

In the US, all federally funded human research is subject to broad-based controls aimed at ensuring all protocols are safe and ethical: Having had the risks explained to them, all subjects must willingly give their informed consent as participants in the research, and before the research protocol is submitted for consideration by the NIH, it must be approved by a local Institutional Review Board (IRB). If institutions stray from these regulations, the NIH, through its federal Office for Protection from Research Risks (OPRR), can withdraw its license to conduct human research. Such suspensions are rare—although the rules have been in effect for more than 30 years, only a handful of institutions have been suspended. However, that may be changing.

In 1998, the OPRR suspended human research for a few days at Chicago's Rush-Presbyterian-St. Luke's Medical Center after discovering that some patients may have been inappropriately persuaded to take part in experiments and that others should never have been asked to participate in the first place. In February of this year, in a more worrying case, the OPRR suspended research at a number of Los Angles-based clinics conducting research under the auspices of Friends Research Institute, citing lapses of the IRB and consent forms that down-played risks and exaggerated benefits. And more recently, in March, the Veterans Affairs hospital, also in Los Angeles, had its human research halted after the discovery that some veterans had been enrolled in research protocols without their knowledge or consent.

Part of the problem lies with the regulations themselves. The detailed rules surrounding human research have remained unchanged for more than 18 years, a period in which technological advances have changed the way that much of human research is conducted, and in which there has been a huge increase in the number of subjects involved—several hundreds of thousands of people now take part in US human research protocols each year.

Thus, even when all the rules and regulations are followed, the system of informed consent and IRB permission is wide open to criticism. A recent report (*J. Am. Med. Assoc.* **280**, 1951–1958; 1998) from the Project on Informed Consent (administered by the Center for Bioethics at the University of Pennsylvania Health System) recommended sweeping changes to the current rules. Although almost no aspect of the rules was left unchallenged, the report focused on three categories of concern: how informed consent can be given by individual subjects with special needs (such as the cognitively impaired); how to improve the effectiveness of the institutional review boards; and policy issues requiring further study (such as the conflict of interest with the OPRR—an NIH office charged with governing all federal human research, the bulk of which is administered by the NIH itself). The government itself also recognizes inadequacies in the current rules. In June of 1998, the Department of Health and Human Services issued a report pointing out weaknesses in the system and characterizing the situation as a "serious national issue."

The problems leading to the Duke suspension focused on the local Institutional Review Boards. The OPRR first visited the Duke campus five months ago and only decided to suspend Duke's license to conduct human research after being disappointed with the slow pace of change made in response to its original criticism. Their more dramatic action of closing down the bulk of the institute's human research (leaving only those trials in which an abrupt cancellation would put subjects at risk) seems to have had its desired effect. Duke's Chancellor for Health Affairs, Ralph Snyderman, acted quickly, immediately committing the organization to correcting any outstanding weaknesses in their procedures.

It is also likely that the OPRR was responding to past criticisms of its ability to regulate and enforce good practices in human research; the Duke action serving as sign of its willingness to take decisive action, and as a 'warning shot across the bows' of the entire US federal biomedical research community.

The OPRR has shown that it is stepping up its vigilance and is prepared to take whatever corrective action is necessary to ensure that human experimentation is held to a high standard. Certainly it should not be afraid to 'bare its teeth' every now and then, if for no other reason that to persuade other institutions not to indulge in the brinkmanship it accuses Duke of. In so doing, it is serving notice that at the center of the biomedical research community is the ability to conduct human experiments. Such experiments require the complete trust of the public and nothing should be allowed to erode that trust.