Vulnerable groups at risk from "commercial" ethical review boards

The rapid increase in private funding for biomedical research is threatening to overwhelm the regulatory system for experiments on human subjects, say bioethicists who testified at a recent Congressional hearing.

The bioethicists are especially concerned by what they see as the growing abuse of institutional review boards, the bodies in universities and hospitals that assess proposed experimental protocols to ensure they are based on sound science and ethics.

Arthur Caplan, a bioethicist from the University of Pennsylvania's Center for Bioethics, told the hearing on research on human subjects that a small but growing number of institutional review boards (IRBs) are now "for hire".This means that a researcher or group of researchers can draw up a contract with a board to review a particular research proposal for an agreed sum of money. Until recently, all IRBs were staffed by volunteers. Although "commercial" IRBs are believed to account for only 2 or 3 per cent of the total of up to 6000 across the United States, Caplan believes they are on the increase.

Normally, IRBs are composed of researchers, clinicians and non-medical people, including community representatives and patient representatives — a mix mandated by the Department of Health and Human Services and the Food and Drug Administration. However, if a group of researchers receives no federal funds, they can invite a group of people, the choice of whom is subject to fewer restrictions, to sit on a "for-hire" IRB. In particular, they need not appoint community representatives and patient representatives.

The existence of such boards creates the potential, says Caplan, for the abuse of research subjects, especially in vulnerable groups such as mentally ill people or children. In one case, he says, scientists studying Alzheimer's disease at a research institute in Georgia decided to take a proposed trial of an anti-Alzheimer drug to a contract IRB in Seattle, which approved the protocol.

But the protocol allowed for non-medical staff to administer the experimental drug, presumably to save money. The trial became "a real mess", says Caplan, because the non-medical staff failed to identify symptoms and certain side-effects of the drug in some participants. "One would expect that an IRB from a distant city, which did not include representatives from the community [and which was unable to] oversee a trial's activities, would be at a distinct disadvantage," said Caplan.

A second problem, said Caplan, is the growing tendency for researchers whose proposed experiments are rejected by their own institution's review board to seek out a more sympathetic board elsewhere, either at another public institution or through a commercial contract. For example, the IRB at Montefiore Medical Center in the Bronx, New York, rejected a proposed trial of a new drug to treat schizophrenia because the protocol required that the participants be taken off their existing treatments while remaining outpatients. The Montefiore IRB considered this "wash-out" period too dangerous to the welfare of the patients. In the end, the researchers took the protocol to a review board at the University of California, Los Angeles, which approved it. One patient who had been withdrawn from medication committed suicide, and the death is now the subject of a court case.

In a separate testimony at the hearing, Benjamin Wilfond, a pediatric respiratory physician at the University of Arizona Health Sciences Center, said that "for-profit" IRBs provide less protection for children than normal IRBs. He cited a study in which asthmatic children had been taken off their medication, so putting them at risk. The trial had been conducted by a private clinician who had arranged for an out-of-state IRB to review the protocol on contract, after his university rejected the protocol. Wilfond called for a ban on all commercial IRBs.

The problems with IRBs are only some of the more extreme examples of abuses in the current system, said Caplan. "A rapidly changing research environment casts doubt on the adequacy of informed consent and IRB review, a lack of basic information about who is involved in research, and inadequate attention to the needs of those who are most vulnerable in research contexts."

Representative Christopher Shays (R-Connecticut), chairman of the Committee on Government Reform and Oversight's subcommittee on human resources, which convened the meeting, said the evidence on IRBs indicated that "the current system of bioethical review appears to be showing signs of age and disrepair". Shays added that "multiple layers of review and enforcement provide a false sense of security that difficult issues are being confronted". He was concerned, for example, about how well trial participants are informed before they consent to participate in trials. "The regulatory scheme lacks specific provisions to protect the mentally ill, drug- addicted and cognitively impaired persons involved in biomedical research."

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American seeds suspected in Japanese food poisoning epidemic

A popular Japanese delicacy, the white radish sprout, is back under suspicion as the cause of the nation's outbreak of deadly *Escherichia coli* food poisoning. But this time investigators are focusing on seeds used to grow the sprouts, imported from the United States.

Radish sprouts are an important part of Japanese cuisine. Last summer, an outbreak of food poisoning among schoolchildren in Sakai City, Osaka, caused by the virulent strain of *E. coli* known as O157, was blamed on them, causing uproar among farmers (*Nature Medicine* 9, 956; 1996). Since last summer, 13 people have died and there have been thousands of cases of illness.

Now the bacteria have been isolated from white radish sprouts linked to three new cases of the illness reported to the Ministry of Health and Welfare since the spring. The cases were in Gamagori, near Nagoya, and in Yokohama. In all three cases, the DNA "signature" of the E. coli O157 that was isolated from the patients was identical to that found in the sprouts, strengthening fears that this food is to blame.