Washington Fax
March 5, 2002

Secret research must adopt Common Rule human subject protections, bioethicists urge

Federal regulations governing classified human subjects research, which by definition must be kept secret for national security reasons, should be implemented as soon as possible, University of Virginia Center for Biomedical Ethics Director Jonathan Moreno, asserted at a "Bioethics and Bioterrorism" conference Feb. 28 in Washington, DC.

"It is likely we will engage in some kind of secret, classified human subjects research in the future, and it seems to me that it borders on the scandalous that we still don't have rules in place that would at least begin to protect the people who are in those trials," Moreno declared at the meeting, cosponsored by his UVA center and the University of Pennsylvania's Center for Bioethics.

In 1996, Moreno explained, the Clinton Administration endorsed recommendations from the Advisory Committee on Human Radiation Experiments, which required the use informed consent, proper security clearances for subjects as well as for institutional review board members, and the maintenance of permanent records of secret human research. (see Washington Fax 9/12/96)

Subsequently, in March 1997 Clinton issued a memorandum giving the relevant federal departments and agencies one year to implement restrictions on classified research, but the process took longer than this allotted time. As of May 2000, 13 of 16 departments and agencies that subscribe to the Common Rule (45 CFR 46) governing human subjects research had signed off on an interim final rule, according to former NIH Office of Protection from Research Risks Director Gary Ellis.

"I personally was reassigned at that time, so I have no knowledge of what happened after that point," Ellis explained; at that time OPRR became an HHS-level office renamed the Office for Human Research Protections.

In order for the rule to move forward and be incorporated into 45 CFR 46, all 17 of the participating agencies would have to sign on, yet two of the agencies that have yet to get onboard are the Department of Defense and Central Intelligence Agency, according to Moreno.

"These rules are still not in place," Moreno continued. "We have now graduated from a time in which we could have a certain amount of bureaucratic lassitude about the possibility that we would ever need to return to a Cold War stance of classified human experiments; I don't think now we have the luxury of that presumption."

In fact, the measure has stalled at 13 signers, OHRP confirms, noting the issue will be reopened at the next meeting of the Human Subjects Research Subcommittee of the National Science and Technology Council's Committee on Science, scheduled for March.

In December 2001 President Bush gave HHS Secretary Tommy Thompson secrecy authority to classify information contained within his department, specifically citing information about the national vaccine stockpiles as in need of protection.

"There ought to be some analysis considering the significance of this; this is the first time, as far as I know, that a health secretary has ever been given classification authority," Moreno stated. "Once an agency gets classification authority, I don't know of any case in which it has it given up."

Further, he explained, the HHS secretary's secrecy authority creates "a whole bureaucracy," involving, for example, development and implementation of criteria for determining which individuals in an agency receive clearance and which kinds of documents or information are classified. In addition, Moreno pointed out, methods must be developed to ensure the security of the protected documents. (see Washington Fax 2/27/02)

As an example of a circumstance under which classified human subjects research could desirable, Moreno pointed to a theoretical situation where national intelligence suspects a certain nation or terrorist group is developing an anthrax strain resistant to current vaccines and antibiotics. In such a case, Moreno said, the U.S. would want to test a new vaccine or drug without the knowledge of the rogue nation or group, and human exposure might be considered since there would be no historic experience with the new agent.

Beyond oversight of secret human subjects research, another issue that emerged as a source of concern at the meeting is the suitability of FDA to oversee research on interventions with national security importance.

"People are in general agreement that the FDA approval process is not designed for national security research," Moreno declared.

For such studies, FDA offers only three possibilities, he said: a consent waiver for a treatment that has been studied as an investigational new drug (IND); an expedited approval process offered under the Bush Administration's Countering Bioterrorism Initiative and a supplemental approval process based on documented prior experience in clinical trials and/or animal studies.

Specifically, the IND issue was addressed by New Jersey State Epidemiologist Eddy Bresnitz. Following the recent anthrax attacks, he said, the vaccine and the antibiotics provided to members of the public suspected of being exposed were only available through an IND protocol, he explained.

Further, the available vaccine, which the military allowed CDC to disseminate, was only approved for preexposure prophylaxis for the military. In addition, while the product is approved as a six dose vaccine, following the anthrax attacks it was only administered in three doses, Bresnitz noted.

"You had a situation where you had preventive measures that you could offer to those exposed, but the problem was that you didn't know whether it worked in that setting; you had to do it under an investigational new drug application, individuals had to sign the informed consent form...which was a six-page document that pretty much allowed the CDC to wash their hands of any adverse effects of the vaccine," Bresnitz remarked.

In New Jersey, he said, about 350 out of over 900 individuals took antibiotics for 60 days and only 49 people agreed to take the vaccine. Nationwide, about 150 people took the vaccine compared to 30,000 who received antibiotics.

"This is going to be an issue for the future," **Bresnitz** asserted. "If there is another anthrax attack, my understanding is that the CDC will be offering the vaccine right from the get-go and also recommending 100 days of prophylaxis."

"Why is that a problem," he asked, "because it will have to be done under an IND protocol, which means you are going to have to sit down and talk with people who have just been exposed to anthrax and say, 'Hey, you were just exposed, we think we have something that will protect you but you are going to have to sign this informed consent form which basically washes our hands of any liability whatsoever.' I think that is a problem, and I think there are some ethical issues in there as well."

In addition, Bresnitz suggested there was insufficient input from the states in developing the consent document provided to these patients. "In the event of another attack," he said, "we are going to have to involve the states - using state employees, state public health officials - to actually do the interaction with the individual, stating benefits and risks; otherwise it will just be a CDC/contractual operation again and if you are talking about not 1,000 individuals but tens of thousands of individuals, CDC can't do it by itself and I am not even sure they have enough contractors to do it or enough money."

Arthur Anderson, U.S. Army Medical Research Institute of Infectious Diseases' Clinical Pathology department chief, suggested the current bioterrorist and national security concerns demand more flexibility in testing and administering protective medical interventions.

Under a memorandum of agreement, between 1964 and 1987 the Army was allowed to protect soldiers with a product the chain of command believed was going to be effective, provided there was safety data in humans and it was deemed the most valuable intervention, he explained. "They could put out into the Vietnam battlefield a plague vaccine, for example, and protect soldiers with an investigational vaccine and report it to the FDA afterwards; no informed consents were necessary, it was treated as though it were licensed."

"I really think in this bioterrorism situation and also in this military situation we need to reestablish this type of memorandum of agreement that allows a contingency license for the period of the event that the product, based on information provided, should be made available as though it were licensed," remarked Anderson, who chairs USAMRIID's institutional review board, known as the Human Use Committee.

"When a particular agent is identified and you need to use a product in an investigational mode, the IRB that handles the protocols most frequently dealing with that subject probably is much better able to have a clear informed consent and better able to make those recommendations," he added. "I think the greatest mistake for IRB-type functions is to have them take place in a politicized atmosphere, and the higher up in government...guarantees that the politicized atmosphere occurs."

On the legislative front, Rep. Diana DeGette, D-CO, is preparing to reintroduce human subjects protections legislation in March. The bill, expected to look similar to the Human Research Subject Protections Act (H.R. 4605) introduced in the 106th Congress, would apply the Common Rule to all human subjects research, regardless of whether it is classified or even federally-funded. (see Washington Fax 6/14/00a)

--Rebecca Spieler

For more on this topic, see our roundup on Protecting human research subjects for related stories and documents.