FDA uneasy about placebo revision

Although not legally binding, revisions to the Declaration of Helsinki regarding the use of placebos in clinical trials have created a stir in the United States Food and Drug Administration (FDA). A senior official has declared the changes wrong both in terms of ethics and science.

The Declaration, drafted by the World Medical Association, outlines ethical practices to be followed in medical experiments with humans. The revised section on placebo use states that all clinical trial patients should receive the best existing therapies and that placebos for control groups are acceptable only when no proven treatments exist (*Nature Med.* **6**, 1198; 2000). This is anathema to the way clinical trials have been conducted for decades.

Although they are under no obligation to implement the current changes, the FDA is concerned about the revision because its regulations require trials conducted outside the US to be in accord with the Declaration's 1975 version. FDA is now pondering to what extent, if any, trial sponsors will be required to comply with the placebo revision.

Robert Temple, director of medical policy at the FDA's Center for Drug Evaluation and Research, vociferously disagrees with the new policy, calling its ethics "bizarre" and its consequences for medicine "a huge loss." In his view, discarding placebo use from clinical trials would effectively end the development of several categories of drugs.

The revised declaration requires non-inferiority trials, in which new drugs must be tested against and proven no worse than established drugs. These studies work for antibiotics and most cancer drugs because there is a clear and large difference between an effective drug and a placebo. But where drug effects are less pronounced, such as antihypertensive, antihistamine, hypnotic and mild analgesic medicines, "the study does not actually work unless it could have distinguished between an active drug and a placebo. And [with the revision] you wouldn't know whether it was capable of doing that because you don't have a placebo," explains Temple. This is why the FDA sometimes refuses to approve drugs for which placebo comparisons are absent.

The new policy, in Temple's interpretation, also effectively precludes approving drugs that improve on older medicines not by being more effective but by having milder side effects. Under the revision, Prozac could never replace the old tricyclic antidepressants, for example. "The declaration just ignores all of these issues, which I consider unpardonable," Temple concludes.

Tom Hollon, Bethesda

West coast US recognizes academic gender bias

The close of last year saw three new cases of potential gender discrimination surface on the west coast of the United States, marking an increase in the attention given to discrepancies in pay and promotion of men and women in academic institutions.

At the University of Washington, a group of female dental school professors has won class action status for their suit which charges that the school pays women faculty less and is less likely to promote them. Gaining class action status is significant because it means that the issue can be argued on behalf of all female faculty, rather than just the four plaintiffs. Catherine Didion, director of the Association of Women in Science, hails the judge's decision against which the school's lawyers are considering an appeal: "It becomes less about the individual and more about the institution."

Biostatistician Sally Blower, who left the University of California at San Francisco (UCSF) last year after alleging gender bias against the School of Medicine (*Nature Med.* **6**, 359; 2000), says, "Class action suits are the way to go. Universities can easily discredit an individual." Following an investigation, UCSF rejected Blower's charges and questioned why she had not made a formal complaint. Blower replies that she took another job and that legal action "would have dragged on for years."

This summer, Blower's new employer, the University of California at Los Angeles, released its own gender equity report, which found little difference in salaries for men and women of the same rank but did find that women were clustered in lower level positions while men were concentrated in higher level positions, such as full-professor and department head.

Moreover, a State senator has ordered an audit of the entire University of California system to examine the apparent decline in hiring women faculty throughout the University of California system. In the past two years, the number of new female faculty hires at the Davis campus has dropped by 50%. A report on the situation is due later this year.

This latest round of activity can be traced to the response to a 1998 Massachusetts Institute of Technology (MIT) report on the status of women, which found that female faculty at MIT felt "marginalized." Since then, the Biology professor who spearheaded the study, Nancy Hopkins, has been inundated by queries from colleagues with similar complaints. Hopkins, who now works part time on MIT's effort to improve conditions for female faculty, has found no easy answers. "The hardest thing is getting people to understand that this is a problem," she says.

The American Association of Medical Colleges acknowledged the issue of gender bias when it set up a women's leadership committee in 1996. But after reviewing new data on female medical school faculty last July, the committee concluded, "On most measures, little progress is occurring." So, women have taken to the courts. Several have filed suits against universities, with mixed results, and these cases exact a huge toll—financially, professionally and personally—says Didion.

Hopkins says that MIT is now looking beyond the numbers at the "processes" that give rise to inequities, but many other schools are still at the data collection stage.

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