Ethics guidelines for clinical trials to be revised

In the wake of ongoing international furor over drug trial horror stories and in hopes of restoring its own fading influence on the global stage, the World Medical Association is proposing to again update its cornerstone statement of ethical principles regarding human experimentation.

To that end, the France-based ethics guardian is seeking input on proposed revisions to the Declaration of Helsinki, which was first developed in 1964 as the medical profession's code of conduct governing the ethics of human research. The Declaration's 11 paragraphs have since been expanded to 32 over the course of 5 revisions, the most recent of which occurred in 2000.

The latest review comes at a time when the pharmaceutical industry's reputation for testing the safety of drugs prior to mass marketing has been in steady free-fall, says Dr. John Williams, the former ethics director of the Canadian Medical Association (1991–2003) and the World Medical Association (2003–2006), who is coordinating the revision process. "Since 2000 there have been so many scandals that have been unleashed that the need for ethical principles, and regulations and laws as well — first of all to be formulated, and second to be applied — is stronger than ever."

Association President Dr. Jon Snaedal of Iceland acknowledges that the proposed amendments are being driven by a desire to re-establish the Declaration's relevance in a world where national and international bodies, like the World Health Organization, have their own far more detailed standards and regulations on ethical trial conduct.

The Association describes most of the proposed Declaration changes as "minor" adjustments, including new wording to stress the rights of trial participants, a call for greater representation of under-represented groups such as children and pregnant women (to ensure companies provide adequate recommended dosages to these groups), and an assertion that "professional" patients who engage in numerous trials for finan-

cial reasons be discouraged. The proposals also echo a chorus of international calls for a public database where details of clinical trials would be registered.

More controversial is a decision by the Association to again wade into the fray surrounding the use of "placebos" in clinical trials. Such use prompted the Association to weigh-in with Declara-

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Clinical trial scandals have prompted the World Medical Association to revise the Declaration of Helsinki, while fears persist that the pharmaceutical industry is moving clinical trials to the developing world because of lax regulation, lower cost and ready access to desperate and often illiterate trial subjects.

tion revisions in 2000, after public outcry erupted over a trial involving HIV-positive women in the developing world. It gave one-half of all participants the drug azidothymidine to determine if a shorter-course treatment would be as, or almost as, effective as the proven longer-course treatment, and the other half a placebo, even though an existing treatment was available. The women in the control group, who came to the trial with the singular hope of sparing their babies the ravages of their own disease, essentially lost a lottery when they ended up getting only a placebo.

Some ethicists defended the trial by arguing that the women would likely have received no treatment had the trial not been conducted. But others recoiled at the notion of a doctor or clinician giving a placebo to a participant that would increase the chances her child could die a horrible death.

That hardened opposition to the Declaration within industry, regulatory

bodies and amidst some academic circles, all of whom argued that such restrictions on placebo use were impractical and would seriously impair research. The Association added "a note of clarification" in 2002 which included the statement that placebo use may be acceptable in some cases, for example, if "necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method."

The new proposals add the caveat that research involving placebos shouldn't proceed unless it's clear patients "will not be subject to any additional risk of serious or irreversible harm." Snaedal says the Association fears loose language could spell disaster in the third world. "If we give leeway on this issue, they will be almost allowed to do anything. Because they can say, 'at least we gave good treatment to hundreds of people'."

Williams argues widespread adoption of the Declaration could restore a measure of public confidence lost as a result of prescription drug debacles and settlements.

The American pharmaceutical industry's lobbying arm, PhRMA, lays some of the blame for that lost confidence at the feet of the media, for having sensationalized "criticisms of clinical trials."

But others argue the industry is the author of its own misfortunes and can't easily shake allegations that, like shoe and clothing companies, it is lured offshore by the equivalent of clinical "sweatshops." In the developing world, companies can take advantage of loose regulations, low costs, rubber-stamp ethics boards and easy access to desperate and often illiterate trial subjects in order to speed up the costly trial process.

"It's been said that (Big Pharma's reputation) is worse than the tobacco industry at the moment," says Dr. Michael Goodyear, an assistant professor of medicine at Dalhousie University. "It's scary stuff. I mean, no matter how much the drug industry protests and complains, they get caught out once a week doing something they shouldn't have done, because there's a lot of money involved and marketing takes precedence." — Peter O'Neil, Paris, France

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