gious US academic institutions such as Duke, Virginia Commonwealth, Johns Hopkins, Pennsylvania and the Fred Hutchinson Cancer Institute, not omitting the sad Poisson breast cancer trial at the University of Montreal.

In the US, the FDA inspects both the private and university teaching hospital REBs. Yet, all the above major problems found by Food and Drug Administration or Office for Human Research Protections inspections have been at academic institutions.

Legitimate differences of opinion will always exist in a free society. Improving the protection of human research subjects is everyone's concern and responsibility — whether a particular study is vetted by an REB in the university/public study sector or private sector.

Jack Corman
President
Morris A. Blajchman
Alternate Chairman
Allan Knight
Chairman
IRB Services
Aurora, Ont.

Reference

1. Weijer C. Placebo trials and tribulations [editorial]. *CMAJ* 2002;166(5):603-4.

Charles Weijer has elegantly discussed the ethical issues regarding the use of placebo controls in clinical therapeutic trials.[1] However, can one speak of placebo-controlled trials when the patient is told that he or she might receive an inactive drug or procedure? A placebo is defined in the *Shorter Oxford Dictionary* of 1811 as "a medicine given more to please than to benefit the patient."[2] Thus a placebo is a pharmacologically inert drug or a dummy procedure prescribed with therapeutic intent. Patients in modern-day clinical therapeutic trials are, by this definition, not given a placebo and cannot be under current guidelines.

The prescribing of a placebo implies deception. Conversely, allocating an inert therapy to a patient who has been instructed that it is inert, with their consent, is quite a different matter. Inert controls provide a greater delta of response than placebo controls.

Currently, the use of placebo therapy is denounced by most ethicists,[3,4] but practising physicians caring for patients find it more acceptable. Why is it deceitful to prescribe a placebo when most modern drugs, especially antirheumatic drugs, are only marginally better and certainly more toxic?[5] Most alternative therapies can be considered super-placebos[6] and are certainly very popular with patients. The greatest placebo is the doctor, a fact appreciated by William Osler.

I hope that the recent National Conference on Appropriate Placebo Use in Clinical Trials, held in Ottawa, was not only attended by scientists, ethicists and policy-makers, but also patients and their families. It is, after all, the patient who is at the end of the final common pathway.

W. Watson Buchanan
Professor Emeritus
McMaster University
Hamilton, Ont.

References

1. Weijer C. Placebo trials and tribulations [editorial]. *CMAJ* 2002;166(5):603-4.
2. Buchanan WW, Bellamy N. The placebo response: clinical efficacy and toxicity. In: *Side Effects of Anti-Inflammatory Drugs IV*. London (UK): Kluwer Academic Publishers; 1977. p. 11-23.
3. Bok S. Ethics of giving placebo. *Sci Am* 1974;231 (5):17-23.
4. Brody H. The lie that heals: the ethics of giving placebos. *Ann Intern Med* 1982;97(1):112-8.
5. Shall I please? [editorial]. *Lancet* 1983;2(8365-6): 1465-6.
6. Joyce CR. Placebo and complementary medicine. *Lancet* 1994;344(8432):1279-81.

[The author responds:]

The point of my commentary[1] is simple: Canada's regulatory system for the protection of research subjects is broken and needs to be fixed. Proof of this failure is found in the approval by 19 out of 20 research ethics boards (REBs) of a placebo-controlled trial that clearly violates article 7.4 of the *Tri-Council Policy Statement* and paragraph 29 of the *Declaration of Helsinki*.[2,3] Effective regulation of research requires change at a variety of levels, including the researcher, institution, funding councils, and Health Canada. It is not surprising that a strong emotional response has been evoked in the letters to the editor. When something is broken, some will continue to insist — however implausibly — that it is working just fine.

Grenier claims that I have not provided sufficient information to determine if the trial in question falls into one of the exemptions laid out in article 7.4. This is not the case. I invite readers to compare the text of my article with article 7.4a-g. This protocol qualifies for none of the listed exemptions.

Corman and colleagues are correct that university and hospital REBs are subject to conflicts of interest because their institutions receive money to conduct research, and researchers often dominate REBs. This is yet another aspect of the current system that needs to be fixed. In 1993, Paul McNeil proposed that REBs ought to be composed of equal numbers of community and institutional representatives, and the REB chair must be a community member.[4] The problem with for-profit REBs cannot, however, be fixed. The REB is a social oversight mechanism charged with the public's trust to protect research subjects. This trust will surely be eroded when the regulatory system contains elements that exist to turn ethics reviews into profit. Corman and colleagues helpfully provide other examples supporting my point that Canada's research regulatory system is broken.

Buchanan reasonably asks whether a placebo given in the context of a modern clinical trial is really a placebo because research participants are informed that they may receive a placebo. A fascinating literature is available on so-called revealed placebo use in medical practice.[5] It is unclear that deception is key to achieving a placebo effect. In any case, placebo use in clinical trials is not fully revealed because subjects are only informed that they *may* receive a placebo, not that they *will* receive one.

Charles Weijer
Department of Bioethics
Dalhousie University
Halifax, NS