

## BRAZIL

# Tough Placebo Rules Leave Scientists Out in the Cold

Brazil's bioethics commission opposes placebos in most multinational trials, despite a shifting stance by the World Medical Association

**RIO DE JANEIRO**—Brazilian psychiatrist Márcio Versiani was hoping to be a co-investigator on a multinational study of patients suffering from panic attacks. The clinical trial is designed to test the efficacy of Efexor (venlafaxine), an antidepressant not yet approved for panic disorders, against an existing treatment, Paxil (paroxetine). A third group receives a placebo, allowing researchers to account for the well-known phenomenon in which some patients respond positively to any medical intervention.

The study is now under way in the United States, Canada, Argentina, Mexico, and Chile—but not in Brazil. Versiani's application last year was one of several turned down by Brazil's federal research ethics commission, CONEP, because of its opposition to the use of placebos in international trials. That hard-line stance has infuriated many Brazilian mental health researchers, who complain that their ability to keep up with the field has been compromised. "We have been off the worldwide clinical research map for a year," says Versiani. But Brazilian officials say they have no plans to modify their position, which stands at one extreme in an ongoing global debate over the use of placebos.

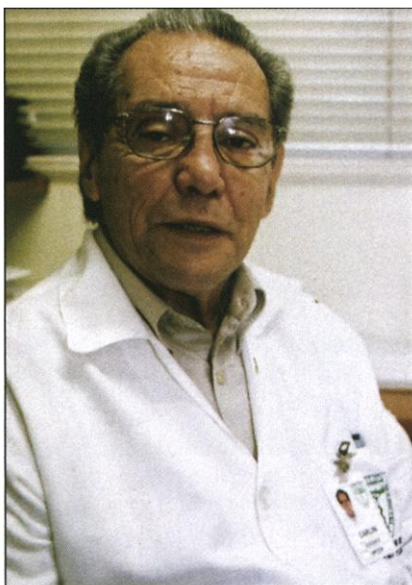
Part of Brazil's National Council on Health, CONEP reviews research projects in areas thought to pose the greatest ethical dilemmas. Among these are the fields of genetics and human reproduction, studies that focus on vulnerable minorities (Indians and the mentally ill, for example), new pharmaceutical products and vaccines, and any research project with humans that involves foreign participation. In 2000 the commission rejected only 17 of 958 research proposals, but 11 of those—some 65%—were denied be-

cause of the "nonjustifiable use of a placebo." Explains Corina Bontempo de Freitas, general secretary of the commission: "From society's point of view, the interest is in knowing if a new drug is better than one that is already known, not if it is better than a placebo."

The commission laid out its views in a March 2000 document prepared for the health council, which operates the commission. It declared that "in any medical trial, all patients, including those in the control group, if there is one, must be assured of the best diagnostic and therapeutic treatment." That stance is similar to a statement adopted in October 2000 by the World Medical Association (WMA), which tightened the 1964 Declaration of Helsinki on patient rights (*Science*, 20 October 2000, p. 418). However, the statement stirred up such controversy that the WMA revisited the issue this fall, declaring that under certain circumstances "a placebo-controlled

trial may be ethically acceptable, even if proven therapy is available" ([www.wma.net](http://www.wma.net)). The exceptions are for "compelling and scientifically sound methodological reasons" or for "minor treatment" that does not subject the patient to additional risk.

Many Brazilian researchers say that the commission's position makes no sense. "It's a return to the days of the caves, an absurdity, a regression," says Elisaldo Carlini, a professor at the Federal University of São Paulo and the first Brazilian to be elected to the United Nations' International Narcotics Control Board. Rejecting such trials has a host of negative consequences, say researchers, from the loss of information about the effects of certain drugs on Brazil's diverse population to a loss of revenue and



**Going backward.** Psychopharmacologist Elisaldo Carlini calls new policy "an absurdity, a regression."

fewer international collaborations. Researchers say that CONEP's rulings also reflect an "ideological bias" against research with foreign partners.

De Freitas denies that there is any such bias and instead argues that scientists need to understand their role in society. "It is not democratic to have some citizens who are considered above suspicion," she says. De Freitas also says that the community is overreacting to the commission's attempt to exercise prudent oversight. CONEP has approved some drug trials using placebos, she notes, such as a recently approved trial to test a new drug for Alzheimer's patients "when there is no alternative for treating the illness."

CONEP's critics include representatives of multinational research companies in Brazil, who say that the country's system for judging the ethics of research protocols is neither objective nor consistent. "If a Brazilian laboratory wants to test a new drug using a placebo group but no foreign partners, this research would not even go before CONEP," says Joao Mas-sud, a physician and medical director for Bristol-Myers Squibb Brasil S.A. Instead, the protocols would be reviewed by ethics committees from the research institution proposing the study.

Others, however, think that the 4-year-old commission is doing a fine job. "CONEP should be a source of pride for the country," says Fabiola de Aguiar Nunes, regional coordinator for the Brasilia office of the Oswaldo Cruz Foundation, an important research center and producer of vaccines and medications in Brazil. "It is protecting our population."

Despite the recent strategic retreat by WMA, Brazilian officials appear to be standing firm. A new bioethics panel was formed last summer to review national policies relating to human cloning and reproduction, transgenic research, biosecurity, and other issues. But it "has no intention of reviewing any [of CONEP's] rulings, nor of addressing the issue of using placebo in international multicenter studies of new drugs," says Cláudio Duarte da Fonseca, science policy secretary for the Ministry of Health, which operates the commission.

Such strongly held views leave Versiani and other researchers gloomy about finding a middle ground in the debate. In the meantime, they say, every passing month adds to the loss of scientific opportunities. "While we watch our national capacity for scientific and technical development stagnate and regress," he says, "the other countries [not excluded from the trials] continue to move forward."

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