the development of private markets in developing countries and "increasing intolerance" for the suffering caused by these infections, making governments more willing to spend their resources on vaccines and treatment. But, he adds, until that time, "the US and Europe will have to make sure all of these products are there when they're needed." Monath adds that US funding of research into a dengue vaccine is not completely altruistic: "This hemisphere is really increasingly threatened by dengue."

OraVax is to begin GMP manufacturing of the first of the four components of their chimeric yellow fever–dengue vaccine, so Monath sees this federal money as coming at a "critical time." He expects to enter clinical trials with the vaccine "in a couple of years." And under the Bayh Doyle Act, the government will have some rights on products developed with their support.

Other grant recipients include SmithKline Beecham in Pennsylvania, which receives $7 million to develop a pediatric indication for an adult antimalarial drug and $1.2 million to develop new TB drugs; New York-based Pfizer will receive $550,000 to study use of azithromycin in combination with antimalarials to treat malaria; Sequella, of Rockville, receives $1.2 million to study new antibiotics against TB; and California-based Aviron receives $2.7 million to develop a new weakened live influenza virus vaccine.

Myrna E. Watanabe,Connecticut

Placebo trials deemed unethical

Two new proposals for the ethical conduct of medical research will push hundreds of clinical trials beyond the bounds of ethical acceptability. The World Medical Association's (WMA) revision of the Declaration of Helsinki and the US National Bioethics Advisory Committee (NBAC) have both called for an end to placebo-controlled trials in developing countries where an alternative standard of care exists. The latter also states that Western researchers and their sponsors have an obligation to provide care to study participants even after trials have ended.

The new declaration language was introduced at a meeting of the WMA in Scotland, UK, last month. The section on placebo-controlled studies now reads that every patient should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods. Placebos are only acceptable when no proven treatment exists.

The change has been prompted by a debate that began in 1997 when Peter Lurie, the deputy director of the Public Citizen Health Research Group, and others challenged the ethics of using a placebo arm in a Ugandan study of mother-to-child human immunodeficiency virus transmission when AZT (3′-azido-3′-deoxythymidine) is used in developed countries to lower transmission rates. The study's defenders argued that placebo studies speed up research—and therefore cures—and that the Ugandan study was appropriate considering that host country's standard of care.

The same study also spurred the NBAC to examine the issue. Its report recommends against the use of a placebo arm in studies of conditions where an effective therapy already exists. Although some have called that approach bad science, the idea received a boost last month with the publication of an equivalence study without a placebo arm that produced new information about mother-to-child HIV-1 *(NEJM.* **343**, 982; 2000).

The report's most striking recommendation states that researchers should "continue to provide to all participants...any research intervention that was proven successful along with other interventions that were provided to participants during the research, if these participants would not otherwise have access to an established, effective treatment."

US researchers told the NBAC that "funding agencies would never be willing to sponsor research that entailed provision of treatment at the end of the study." If cost is the issue, it shouldn't be, says Lurie. "These are multimillion dollar trials funded by enormous government agencies or multibillion dollar pharmaceutical companies," he said. "They can well afford to provide these interventions to the very people who have put their health on the line for the companies."

Money is not the only issue, says Sara Radcliffe of the Pharmaceutical Research and Manufacturers Association, an industry lobbying group. In the right situation, pharmaceutical manufacturers are willing to continue providing treatment, and some do, she says. But if that were a requirement, it might do more harm than good. For example, many countries won't be able to ensure antibiotics are used in a way that prevents an increase in resistance. Ultimately, she says, "It seems problematic to make drug companies responsible for making up for shortfalls in health care delivery."

Although highly respected as guiding principles for medical research, neither the NBAC report nor the declaration is legally binding.

Tinker Ready, Boston

Brazilian studies supported long-term

The State of Sao Paulo Research Foundation (FAPESP), the most important state research foundation in Brazil with a budget second only to the National Research Council, has singled out six major biomedical research centers for long-term support. Facilities devoted to human genome research, structural molecular biotechnology, cancer research, applied toxinology, cell-based therapy and sleep studies will receive funding for up to 11 years, with review after 6 years. FAPESP will supply materials and staff.

Mayana Zatz, coordinator at the Human Genome Center at Sao Paulo University, says that they hope to increase "understanding of the most prevalent genetic diseases in Brazil as well as the ethnic complexity of mixed and isolated Brazilian populations such as Amazonian Indians."

Glacius Oliva, who directs Structural Molecular Biotechnology at the University, intends to use FAPESP funding to boost research into diseases inherent to Brazilians, such as Chagas' disease, leishmaniasis and yellow fever, but neglected by the international community.

At the Center for Applied Toxinology at the Butantan Institute where bradykinin was discovered in 1949, research focuses on compounds derived from naturally occurring toxins from snake venom, insect-bites and pathogens. Center director, Antonio Carlos Martins de Camargo, says that work will focus on antihypertensive and vasodilator drugs, anticoagulant factors and neurotoxins. Brazil has never developed a proprietary drug.

Xavier Bosch, Barcelona