OECD MEETING

CRITERIA FOR LOW- TO NO-RISK FIELD TRIALS

PARIS—Many field trials involving the deliberate release of organisms into the environment are designed to be done under conditions that present negligible or low risks. Establishing the actual scientific criteria for such experiments is a major priority of the Organisation for Economic Cooperation and Development's (OECD) Group of National Experts on Safety in Biotechnology.

Meeting here in April, the Group drafted a working document of criteria for implementing Good Developmental Practice (GDP) for small-scale field testing. The document will be refined by a U.S.-led OECD working party, which hopes to perfect it by the end of the year.

Of the criteria that must be considered in determining the risk category of field trials involving plants, the most important is the plant's reproductive capacity. The safest trial imaginable would use plants that can grow in reproductive isolation. This would ensure that such plants could not transfer genetic information to any pre-existing plants at the test site. If the plants cannot be grown in reproductive isolation, they must be grown under conditions that are functionally equivalent. Reproductive isolation can be achieved in a number of ways, including using annuals that have no means of vegetative reproduction, or choosing a plant that is sexually incompatible with its neighbors.

To meet GDP criteria for field testing, plants must satisfy the following requirements, as well: The plant must not have been modified to produce a toxin it does not normally make, except that if the plant *has* been modified to make a toxin, proof that the organism has no known potential to negatively affect the ecosystem is required. Any of the following conditions will provide that proof: there is a history of the organism's safe uncontained use in an environment similar to the test site; there is an intrinsic, biological limitation on the organism's growth in the test site; or there is evidence that the likelihood of disseminating the organisms under the conditions of the field trial is minimal.

If a vector has been used to construct the plant, the vector's DNA must be well-characterized and unlikely to be transmitted horizontally. If the DNA is derived from a plant, that plant must either be the same species as the host, or closely related. If the DNA is from a prokaryote or a lower eukaryote, those organisms must be non-pathogenic. If the DNA is derived from a plant pathogen, all "harmful" sequences must be deleted. Chimeric vectors should satisfy the same criteria.

Small-scale trials involving microorganisms deal with significantly larger populations than do those using plants. Accordingly, containment procedures become more important than for plants. Still, the primary consideration in evaluating a proposed field trial would be the microorganism's abilities to spread from the test site, to transfer genetic material horizontally, to persist in the environment, and to affect the environment adversely. To demonstrate that the microorganism will not be detrimental to the environment, the same criteria apply as do for plants—a history of safe, uncontained use; an intrinsic limitation on its growth in the test site; or evidence that the likelihood of dissemination is minimal.

The GDP criteria also require an assessment of how the introduced microorganism—be it wild-type or modified—might affect other organisms and the environment. Modified microbes must meet all the following criteria: the introduced trait(s) should not increase the organism's host range nor its antibiotic resistance; and—as with plants—if the microorganism *does* produce a toxin, this toxin must have no known potential for adversely affecting the environment.

The OECD's working draft on GDPs is merely a starting point: progress towards international concensus requires that member countries participate in establishing the criteria necessary to evaluate minimal risk environmental releases.

The establishment of criteria for low- or minimal-risk organisms for field tests will undoubtedly be embraced eagerly by a number of national regulatory authorities as they struggle to balance R&D against the need to protect human health and the environment. It is not far-fetched to expect that such generic criteria will provide large categories of regulation-exempt field trials.

—Jennifer Van Brunt

RABIES VACCINE

A CONTROVERSIAL TEST CASE

WASHINGTON, D.C. and CARDIFF, Wales—A rabies vaccine trial conducted in 1986 at a Pan American Health Organization (PAHO) test facility in Argentina has been controversial from the start (see *Bio/Technology* **5**:13, Jan. '87). Delivering a paper at REGEM 1 on behalf of Jose La Torre from Argentina's Animal Virology Center (Serrano), Faustino Sineriz added new accusations.

Scientists from Argentina now charge that the vaccine caused minor health effects in several humans. Indeed, they assert that the experiments on cattle were aimed covertly at assessing the new rabies vaccine's safety among Argentinean animal caretakers working at the PAHO center. According to the report prepared by La Torre, the live, recombinant, vaccinia-based rabies vaccine "passed from the vaccinated animals to all of their contacts and at least in two cases to the humans directly handling [them]."

Researchers from the Wistar Institute (Philadelphia, PA), who helped develop the experimental vaccine, say that the new accusations do not make scientific sense and that the whole matter should be submitted to an international commission of experts. "According to the data we know, 30 days after the test was begun, the [inoculated] animals developed antibodies...but the controls and handlers did not," says veterinarian Charles Ruprecht of Wistar. And after numerous laboratory studies, he adds, there is "little reason" to think that secondary transmission occurs, either between inoculated and untreated animals or lab personnel. Secondary transmission, which might be an asset for the vaccine in treating wildlife, remains "very difficult to achieve" even among animals kept in close contact in the lab, he says. Such inconsistencies "cast doubt on the veracity of the Argentine allegations," another Wistar official notes.

Meanwhile, the experimental vaccine has been tested in about 15 different species and in hundreds of animals. One field study to immunize wild foxes against rabies began in October 1987 at a military base in Belgium. In addition, Wistar scientists and their collaborators at Transgene (Strasbourg, France) recently submitted a proposal to the U.S. Department of Agriculture (USDA) to test the vaccine in wild animals on several uninhabited islands off the coast of Virginia or South Carolina. If approved, the trial could begin in late 1988.

—Jeffrey L. Fox