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COVER The southwestern shore of Lake Nyos in Cameroon after the toxic gas disaster in August 1986 which killed an estimated 1700 people and several thousand livestock. A fountain of water created by the release of an estimated 1.0 cubic kilometer of gas washed over an 80-meter rock promontory causing a 90-centimeter drop in the lake's water level. See page 169. [Michael A. Clark, Armed Forces Institute of Pathology, Washington, DC 20306]

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The Case for Qualifying "Case by Case"

A recurring theme in discussions of governmental oversight of "deliberate releases" of genetically engineered organisms concerns precisely what classes of organisms should be regulated. The experiments "captured" by governmental regulation should be only those that are necessary and sufficient to protect human health and the environment. Related to this theme is the phrase "case by case," as in "ensure that recombinant DNA organisms are evaluated for potential risk, prior to applications in agriculture and the environment by means of an independent review of potential risks on a case-by-case basis."* The concept of case-by-case evaluation of proposed field trials by national authorities is widely touted and has become something of a totem, inspiring much reverence but little reflection. Evaluation of each and every proposed field trial would be contrary to accepted practice, debilitating to academia and to industry, and an unnecessary burden to government.

In the quotation above, from a recently published Organization for Economic Cooperation and Development document, case by case was carefully qualified to mean specifically "an individual review of a proposal against assessment criteria which are relevant to the particular proposal; this is not intended to imply that every case will require review by a national or other authority since various classes of proposals may be excluded." Thus, in current practice, an investigator contemplating a field trial reviews, or compares, the various aspects of his experiment with relevant assessment criteria to determine whether prior governmental approval is required. For example, if the experiment were a field test of ore extraction by an indigenous *Thiobacillus* manipulated with recombinant DNA techniques in order to delete a gene, the review performed by the investigator would reveal that both the National Institutes of Health Guidelines and the relevant Environmental Protection Agency regulations (under the Toxic Substances Control Act) exempt the experiment from prior approval.

The OECD qualification of case by case underscores the important principle that categories of products entailing negligible or trivial risk may be defined so as not to require special governmental scrutiny or restriction; these could range from narrow products (for example, an inclusive list of such organisms as *Pseudomonas syringae, Bacillus thuringiensis*, and *Thiobacillus ferrooxidans*, manipulated by self-cloning) to broad ones (for example, all well-characterized nonpathogens). This principle of exemption of low-risk categories is, after all, nothing new: more than 90 percent of recombinant DNA laboratory experiments potentially under the jurisdiction of the NIH guidelines have been exempted completely, and the NIH Recombinant DNA Advisory Committee has begun to create categorical exemptions from the definition of "deliberate release."

Perhaps the most compelling argument for a qualified definition of case by case is the extraordinary safety record of field testing of live microbial pesticides that, until recently, could occur unencumbered by federal regulation. At least 13 organisms, approved and registered with EPA, are marketed in dozens of different products.† All of these (as well as numerous other unsuccessful candidates, undoubtedly) were developed and field tested safely without regulatory oversight, because field trials on less than 10 acres were then exempt from the Federal Insecticide, Fungicide, and Rodenticide Act, the pesticide statute.

Consider, in addition, the monumental successes of pre–recombinant DNA genetic engineering of "deliberately released" products such as high-lysine corn, disease-resistant wheat, and genetic hybrids such as tangelos, beefaloes, and a vast array of flowers. Should every field trial of a new variety of these require the imprimatur of the federal government? Should the use of recombinant DNA techniques per se to effect a genetic change determine the need for federal oversight? Obviously not, but one might well wonder, hearing the uncritical clamor for "case-by-case" approvals of all "deliberate releases."—HENRY I. MILLER, *Special Assistant to the Commissioner, Food and Drug Administration, Rockville, MD 20857*

*Organization for Economic Cooperation and Development, *Recombinant DNA Safety Considerations* (Paris, France, 1986). †F. Betz, M. Levin, M. Rogul, *Recomb. DNA Tech. Bull.* 6, 135 (1983).