Letters

Recombinant DNA: International Guidelines

In his News & Comment briefing (17 Oct., p. 280) describing the new publication from the Organization for Economic Cooperation and Development (OECD), "Recombinant DNA safety considerations" (*1*), David Dickson captured some of its important, broad conclusions and recommendations, but, quite literally, missed some essential fine print.

The OECD document considered various aspects of the safety of recombinant DNA techniques employed to manipulate organisms for use in industrial facilities and for environmental and agricultural applications. As related accurately by Dickson, the OECD Council (in the recommendation of the document) suggested "that the risks of releasing organisms containing recombinant DNA into the environment be evaluated on a 'case-by-case' basis." However, in footnotes, both the document and the Council meticulously defined "case-by-case" as "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*" (emphasis added). This definition establishes the important principle that categories of products entailing negligible or trivial risk may be defined that do not require special governmental scrutiny or restriction; these could range from narrow (for example, an inclusive list of such organisms as *Pseudomonas syringae* and *Bacillus thuringiensis*, manipulated by self-cloning) to broad (for example, all well-characterized nonpathogens). Thus, whole categories could be exempted from any significant degree of regulatory oversight. This principle is, after all, nothing new. More than 90% of recombinant DNA laboratory experiments potentially under the jurisdiction of the National Institutes of Health Guidelines have been exempted completely, and the NIH Recombinant DNA Advisory Committee (RAC) has recently recommended a category exempt from the definition of "deliberate release" (News & Comment, 10 Oct., p. 146). Of even greater relevance 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 the Environmental Protection Agency, are marketed in 75 different products (*2*). All of these (as well as numerous other unsuccessful candidates, presumably) were developed and field-tested safely without regulatory oversight, since field trials on less than 10 acres were then exempt from FIFRA (Federal Insecticide, Fungicide, and Rodenticide Act), the pesticide statute.

Moreover, we would have wished that Dickson convey more of the salient conclusions of the document that have caused it generally to be perceived as progressive. For example, the document summary (*1*, p. 41) noted that

> the means for assessing rDNA organisms can be approached by analogy with the existing data base gained from the extensive use of traditionally modified organisms in agriculture and the environment generally. With step-by-step assessment during the research and development process, the potential risk to the environment of the applications of rDNA organisms should be minimised.

The real value of the OECD document is, we believe, not simply that it articulates useful principles for the oversight of organisms manipulated by recombinant DNA techniques, but that it places new biotechnology in perspective; that is, as an extension, a refinement, of conventional biotechnology applied to industry, agriculture, and the environment, with which we have substantial experience and success.

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REFERENCES

1. "Recombinant DNA safety considerations" (Organization for Economic Cooperation and Development, Paris, 1986).
2. F. Betz, M. Levin, M. Rogul, *Recomb. DNA Technol. Bull.* **6**, 135 (1983).

Growth Hormone Use

Before the Food and Drug Administration approved the use of Protropin growth hormone, the limited supply of human pituitary growth hormone hindered advancement of our understanding of growth hormone's biochemical action as well as the scope of its medical application (Research News, 3 Oct., p. 22). Now that supply is not the problem, the next few years will witness an intense effort to redefine the parameters of growth hormone deficiency. This effort should also result in the recognition of those forms of short stature that will not respond to growth hormone.

The physiologic responses to growth hormone in growing children, including improved nitrogen retention, may well have potential uses in other areas of medicine such as tissue repair, nutritional deficiencies, and growth-hormone-deficient adults. The common assumption that adults have no further need for growth hormone has not been examined, in part, because supplies of growth hormone have been inadequate. These possible benefits and the demonstration of the safety of growth hormone use in these situations will require intensive, controlled clinical studies. These are important medical advances resulting from biotechnology, not "cosmetic endocrinology."

There will always be those who will try to exploit major scientific advances for trivial or cosmetic purposes. This should be discouraged and Genentech is committed to limiting the use of growth hormone to proven and approved indications. It is not at all clear that growth hormone has a role in the treatment of obesity. Certainly, there is no reason to expect that it will have any beneficial effect in the absence of an effective program of weight loss.

When Genentech began development of growth hormone, the market was perceived as a small one. Genentech persevered because we felt that safety and supply were important issues. Our primary commitment remains the effective treatment of children with growth hormone deficiency. At the same time, we will work with our scientific collaborators to explore carefully the full range of applications of growth hormone that may be of legitimate and ethical medical benefit.

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A note of caution should be added to Gina Kolata's report of a "New growth industry in human growth hormone?" The article reported a cosmetic anti-aging effect of growth hormone (GH) making it "logical to postulate that some of the changes in aging are related to the fact that growth hormone is not around to the extent that it originally was" (quote attributed to Robert Blizzard of the University of Virginia Medical Center). This statement should be balanced by extensive data that suggest that GH may have effects that accelerate aging (*1*).

As an example, in acromegaly, the adult syndrome of excess growth hormone production, there is a diffuse neuromyopathic process with weakness involving proximal muscles. In addition, GH excess is associated with a high incidence of cardiomyopathy, hypertension, diabetes, atherosclerosis, coronary disease, and osteoporosis (*2*). Growth hormone may be hypersecreted in diabetes, but GH-deficient dwarfs with mild diabetes