Letters

Fenfluramine Studies

While we were not, to our knowledge, approached for comment before Deborah M. Barnes' Research News article "Neurotoxicity creates regulatory dilemma" appeared (6 Jan., p. 29), as the manufacturer of fenfluramine, we are at this time pleased to present more information to the reader.

First, it has been established that fenfluramine, unlike MDMA (3,4-methylenedioxymethamphetamine, or "ecstasy"), does not possess abuse liability and does not produce physical dependence. Although Barnes likens fenfluramine to amphetamine derivatives, fenfluramine's behavioral and pharmacological effects in animals and humans are very different from those of amphetamine-like agents. In therapeutic doses, fenfluramine, unlike most amphetamine derivatives, does not affect norepinephrine and dopamine neurochemistry. As the World Health Organization stated in 1980, "There is evidence that this drug [fenfluramine] does not have amphetamine-like abuse liability nor is there evidence of significant public health and social problems . . ." (*1*).

Second, clinicians have safely prescribed fenfluramine for more than 25 years, in 90 countries, including the United States, to more than 50 million patients, for the treatment of obesity. We have continuously monitored the clinical efficacy of this drug and have carefully scrutinized reports of adverse effects. The most common side effects are sedation and mild gastrointestinal disturbances. Numerous double-blind studies have demonstrated that fenfluramine greatly benefits patients such as obese diabetics, who must reduce their body weight for medical reasons.

Third, 11 years ago, research reports suggested that parenteral administration of high doses of fenfluramine to rats caused destruction of brainstem serotonin cell bodies. After careful investigation, an advisory committee of the U.S. Food and Drug Administration (FDA) concluded, "There are probably no true pathological changes that can be identified in any rat studies" (*2*). The state-of-the-art methods used in the most recent studies alluded to by Barnes confirm the FDA's findings, that is, fenfluramine in tremendously high doses does not result in the loss of serotonin cell bodies.

Finally, current studies on fenfluramine, particularly those cited by Barnes, call for commentary. The kinetics and metabolism of fenfluramine depend on species, dose, and route of administration. For example, a dose of 40 milligrams per kilogram given subcutaneously in rats leads to a drug brain exposure 700-fold greater than does a pharmacologically active dose of 1 milligram per kilogram given orally.

Under these circumstances, we believe the relevance of the current animal studies to patients who are prescribed fenfluramine is highly speculative.

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REFERENCES AND NOTES

1. *Review of Psychoactive Substances for International Control* (World Health Organization, Geneva, 1980).
2. "Report of Peripheral and CNS Drugs Advisory Meeting," 13 June 1978 (Food and Drug Administration, Rockville, MD, 1978).

Climatic Change and Forests

A recent exchange of letters (30 Sept., p. 1736) discussed the possible interactive effects of climatic change on the world's forests. The letter by Roger A Sedjo (p. 1737) cited, but perhaps misinterpreted, my work.

First, it is not my work but rather that of Kauppi and Posch (*2, 3*) which suggests that the growth rates of boreal forests might increase under a doubled CO_2 scenario, and in some areas more than the 75% to 100% cited by Sedjo. The Kauppi-Posch results derive from an empirical regression relation between effective temperature sum and average annual tree growth observed in data from 19 forest districts in Finland. Of course, growth response might differ between managed and unmanaged forests (*4*) and across other parts of the boreal zone.

Recognizing this as a slim basis for extrapolation to the entire boreal zone, I attempted to verify the Kauppi-Posch model for the six regions used in my analysis: eastern and western Canada, Finland, Sweden, Norway, and the U.S.S.R. Kauppi and Posch (*3*) used data on the current climate to estimate current forest growth rates on a grid 5° E-W and 4° N-S covering the Northern Hemisphere between 38°N and 70°N. I aggregated these point estimates of forest growth to average values for the relevant political units and compared these averages with reported information on the actual rates of forest growth (*1*, p. 211 and table 6.2). Deviations between estimated and actual growth ranged from −0.08 cubic meter per hectare per year (−0.9%) in Finland to 0.89 cubic meter per hectare per year (29.6%) in Sweden. In five of the six regions the deviations were positive. This suggests that the Kauppi-Posch model tends to overstate forest growth when extended to large regions outside Finland, but the margin of error is less than the estimated impact of a doubled CO_2 climatic change.

Second, the changes in forest area quoted by Sedjo overstate what might be expected. His analysis assumes that an "expanded global area of boreal forest" of "approximately 6×10^6 square kilometers" represents an area *additional* to the extant forest. This is not the case. As I clearly state (p. 209), my calculations are for *exploitable* forest area, that is, land with forest growth greater than 0.5 cubic meter per hectare per year. In the discussion of the doubled CO_2 scenario, I further indicate, "In no case [that is, in none of the six regions] does the calculated increase in exploitable forest area under climate warming exceed the current total forest area of the country" (*1*, p. 210). Thus the principal effect anticipated by my calculations is an increase in growth, not an increase in forest area as an ecologist would define it.

While I agree with Sedjo that CO_2-induced climatic warming could conceivably produce some homeostatic response within the biosphere, we should be quite humble about our capability to estimate the magnitude of this effect. Humility is, of course, no excuse for ignoring the problem. My examination of the issues, conducted in 1985, was an early attempt to integrate ecological and economic response models to study the effects of climatic change on the world's forest sector. No doubt better data, better scientific knowledge, and better models will give more reliable results.

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2. P. Kauppi and M. Posch, *Clim. Change* 7, 45 (1985).
3. ——— in *The Impact of Climatic Variations on Agriculture*, vol. 1. *Assessments in Cool, Temperate and Cold Regions*, M. L. Perry, T. R. Carter, N. T. Konijn, Eds. (Kluwer, Dordrecht, 1988), chap. 5.
4. C. S. Binkley and B. C. Larson, in *Forest Decline and Reproduction: Regional and Global Consequences*, L. Kairiukstis, S. Nilsson, A. Straszak, Eds. (Working Paper WP-87-75, International Institute for Applied Systems Analysis, Laxenburg, Austria, 1987), pp. 223-230.

Financial Benefit from Research

As I understand the charges directed toward Scheffer C. G. Tseng (News & Comment, 16 Dec., p. 1497), he is in trouble because he conducted nonfraudulent re-