be unique to high doses. It also states that risk assessment is an "area of science that is relatively new and constantly changing . . ." and that current practice "provides an opportunity for scientific scrutiny, which we welcome as a framework for evaluation and improvement." Our papers should be seen within the context of that scientific scrutiny and evaluation. We recognize that current regulatory procedures are grounded in peer review of methods and practice. Our view is that the consensus that developed in the 1970s was based on assumptions that recent evidence suggests are wrong. The high proportion of carcinogens among chemicals tested at the maximum tolerated dose (MTD) emphasizes the importance of understanding cancer mechanisms in order to determine the relevance of rodent cancer test results for low-dose human exposures. A list of rodent carcinogens is not enough.

The EPA letter states that, when confronted with alternative risk projections that current data do not resolve, "EPA assessments employ the assumption basic to all toxicological evaluation that effects observed in animals may occur in humans and that effects observed at high doses may occur at low doses, albeit to a lesser extent." The main rule in toxicology, however, is that "the dose makes the poison": at some level, every chemical becomes toxic, but there are safe levels below that. A consensus developed in the 1970s that we should treat carcinogens differently, that we should assume that even very low doses might cause cancer; this consensus was based on the precedent of radiation, which is both a mutagen and a carcinogen; radiation gave credence to the idea that there could be effects of chemicals even at low doses although we lacked the methods for measuring such effects. This idea evolved because it was expected that (i) only a small proportion of chemicals would have carcinogenic potential and (ii) testing at high dose would not produce a carcinogenic effect unique to the high dose. In our papers and replies to letters in *Science*, we have discussed in detail the accumulating evidence from a variety of disciplines suggesting these assumptions are wrong and therefore that it is time to re-evaluate them.

The risk assessments on which regulations are based are not scientifically justified. Testing chemicals for carcinogenicity at near toxic doses in rodents does not provide enough information to predict the numbers of human cancers that might occur at low-dose exposures. We have discussed the importance of ranking possible carcinogenic hazards and the uncertainties in risk assessments (*5*). Therefore, the public might be better served if EPA were to present its risk assessments as comparisons to its estimates of risks from cups of coffee, beers, and so forth, given the enormous natural background of potential rodent carcinogens.

The EPA letter points out that not all assumptions used in their risk assessments are conservative, for example, the potential synergistic interactions among chemicals. We agree that some interactions can potentiate carcinogenesis; however, interactions can also be inhibitory, and at low doses defenses in humans are usually inducible. The main conservative assumption is that the effects of mitogenesis at high doses can be ignored in low dose extrapolations.

With respect to regulatory policy, the EPA letter states that if current regulatory limits were not in place then higher levels of synthetic chemicals might be found in air, water, and food. Our papers do not argue to discontinue regulation nor, as EPA misrepresents us, to allow "unrestricted additions of pesticides to the food supply." Regulation involves trade-offs, and the best science is necessary so that regulation does not become counterproductive. We have discussed these important trade-offs (*1*).

BRUCE N. AMES
Department of Molecular and Cell Biology, University of California, Berkeley, CA 94720
LOIS SWIRSKY GOLD
Carcinogenesis Potency Database, Lawrence Berkeley Laboratory, Berkeley, CA 94720

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Erratum: In Marcia Barinaga's article "Was Paul Biddle too tough on Stanford?" (News & Comment, 11 Jan., p. 157), the photograph of Paul Biddle on page 157 should have been credited to Damian Marhefka.

Erratum: In the 21 December response by Bruce N. Ames and Lois S. Gold (Letters, p. 1645) to the letter by Frederica P. Perera (p. 1644), the last sentence of the third paragraph in column three should have read, "Both natural arsenic in water and natural radon in indoor air are present at high levels at some locations and were long neglected, while major efforts were put into miniscule amounts of industrial pollutants." In the 4 January response by Bruce N. Ames and Lois S. Gold (Letters, p. 12) to the letter by David P. Rall (p. 10), reference 11 should have read, "D. G. Hoel, J. K. Haseman, M. D. Hogan, J. Huff, E. E. McConnell, *Carcinogenesis* **9**, 2045 (1988)"; reference 14 should have read, "E. Marshall, *Science* **250**, 900 (1990); R. Doll, *Eur. J. Cancer* **26**, 500 (1990); C. Hill, E. Benhamm, F. Doyon, *Lancet* **336**, 1262 (1990); S. Freni, *ibid.*, p. 1263."