grammed cell death. The institution of dietary restriction at a level that will reduce or delay the appearance of tumors and extend life span will thus provide a test animal that will be far different in its responses to drugs and toxic agents than that which has been used as a standard for the past 40 to 50 years. Any change from the ad libitum–fed animal to one kept on any degree of dietary restriction should be preceded by a careful and extensive set of comparison studies for the two conditions in all categories of drugs or toxic agents to be tested. The underlying response baselines will have been strongly altered at several levels, and not necessarily to the same degree for each category.

As for test animal-versus-human comparisons, we should remember that there are a great many more ad libitum–fed, obese Americans out there than dietary restricted ones.

Norman S. Wolf
Department of Pathology,
University of Washington
School of Medicine,
Seattle, WA 98195, USA

References

1. R. W. Hart, D. A. Neumann, R. T. Robertson, Eds., *Dietary Restriction: Implications for the Design and Interpretation of Toxicity and Carcinogenicity Studies* (ILSI Press, Washington, DC, 1995), pp. 127–140, 167–196, 213–228, and 245–326.

Tamoxifen Ruling in California

The decision in May to list tamoxifen as a carcinogen in California was not "preliminary," as stated in the ScienceScope item "Anticancer drug under scrutiny as carcinogen" (6 Oct., p. 19), but was simply the expert committee decision required by Proposition 65. It was based, like all such decisions, on the weight of available peer-reviewable evidence. The finding was made at a public meeting, held to review the literature and consider information believed by any member of the public to be pertinent. Legal counsel representing Zeneca Pharmaceuticals, tamoxifen's manufacturer, indicated at that meeting that the company did not challenge the finding that tamoxifen use is followed by and is likely to cause endometrial cancer. The predominant concern expressed by Zeneca's representatives, appropriately, was in relation to the occurrence of other, particularly gastrointestinal, neoplasms.

There is no intent to "deliberate for 6 months" before making a final decision; the original decision was intended to stand. It now is presumed that the compound will be listed unless additional information submitted by 31 October shifts the weight of evidence. Any compound listed can be removed from the list should stronger pertinent information to the contrary become available at a later date.

This legally mandated process of hazard identification does not address the issue of the compound's net benefit. Important commercial chemicals are listed, as are useful and widely used (and accepted) drugs, including chemotherapeutic agents, analgesics, and a best-selling formulation, conjugated estrogens. Evidence that neoplasms are produced in humans under conditions of treatment makes the listing of tamoxifen unavoidable.

Doctors who make case-by-case medical decisions weigh the costs against the benefits and, with the help of informed consent, allow the recipient of an agent to review the decision. Others who distribute carcinogenic chemicals may be less prudent. In the larger context of informing the public (in this case at the voters' request) about all the carcinogens they may come in contact with, it should be the duty of industry and consumer representatives to provide the most accurate information available, and it is the inescapable duty of government to digest and summarize that information with as much insight and objectivity as can be mustered. Insight and objectivity are often enhanced by outside scientific advisers,

who will not make themselves available unless they think their expertise will count for something. It is said that laws are like sausages: seeing what goes into them destroys one's confidence in them. Scientific judgments made on behalf of the public must not come to that.

Thomas Mack
Department of Preventive Medicine, University of Southern California School of Medicine, Los Angeles, CA 90033, USA, and Chairman, Carcinogen Identification Committee, Office of Environmental Health Hazard Assessment, California Environmental Protection Agency

■

Lyme Disease Study

Eliot Marshall's News & Comment article (13 Oct., p. 228) concerning the National Institutes of Health's (NIH's) study to settle the dispute concerning Lyme disease was a relief to many on both sides of this controversy. To ensure that this debate is settled fairly and convincingly, both sides should be fully represented and deeply involved in the planning and design of the study, and both should agree formally about the protocol—before the results are in. Both sides should agree on what specific results would support which side of the debated issue. Statistics should be involved in the design, analysis, and interpretation, and at least one of them should be outside the medical community.

The analysis should not be based on only the standard results of hypothesis tests and their associated problems (for example, the arbitrary α level, the multiple testing problem, or assumed asymptotic distribution of the test statistic). I suggest the use of an informational theoretic approach to inference, such as Akaike's information criterion, in addition to the traditional testing approach. With these caveats, I hope the study is funded and conducted.

David R. Anderson
77 Breakwater Drive, Fort Collins, CO 80525, USA
E-mail: anderson@picea.cnr.colostate.edu

■

Glucocorticoids

Jean Marx describes the discovery of interaction between the transcription factor NF-κB and the glucocorticoid receptor in her Research News article "How the glucocorticoids suppress immunity" (13 Oct., p. 232). Readers may incorrectly conclude that this observation was simultaneously made by four laboratories a year ago. Our description (*1*) of a direct interaction between NF-κB and the glucocorticoid receptor, which established NF-κB as a target in anti-inflammation, was published almost 2 years ago. A year later, Scheinman *et al.* and Caldenhoven *et al.* reported similar data (*2*). We believe that existing evidence does not allow a generalized assumption that upregulation of IκBα production is *the* major pathway by which glucocorticoids repress NF-κB–mediated activation of all target genes by all stimuli. An interaction between NF-κB and the glucocorticoid receptor appears to play a significant role in the rapid and efficient transcriptional repression of the inflammation-associated cytokine interleukin-6 gene by glucocorticoids.

Anuradha Ray
Department of Internal Medicine, Yale University School of Medicine, New Haven, CT 06520–8057, USA

References

1. A. Ray *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **91**, 752 (1994).
2. R. I. Scheinman *et al.*, *Mol. Cell. Biol.* **15**, 943 (1995); E. Caldenhoven *et al.*, *Mol. Endocrinol.* **9**, 401 (1995).