Correspondence

"E-biomed" and Clinical Research

To the Editor: In his editorial (June 10 issue),[1] Dr. Relman recommended a cautious approach to the proposal for sponsorship by the National Institutes of Health (NIH) of a Web site for the publication of all new biomedical-research reports. However, the NIH proposal is considered by many to be overdue. Dissemination of the results of clinical research on the Internet is inevitable. The question is, who will publish them first? My preferences would be a high-quality, peer-reviewed site under the leadership of a publicly funded institution, such as the NIH. The advantages of this type of sponsorship are strong credibility in international science and health, an international reach that exceeds that of most organizations, and independence from commercial support.

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1. Relman AS. The NIH "E-biomed" proposal — a potential threat to the evaluation and orderly dissemination of new clinical studies. N Engl J Med 1999;340:1828-9.

To the Editor: The advent of on-line publishing appears to be blurring the distinction between journals and data bases. Although this development may have some potential drawbacks with respect to journal review and financing, we see one major advantage: on-line resources, such as "E-biomed," would allow scientists and clinicians access to a more detailed archive of data than is available in print journals. Increasingly, scientific and clinical papers are associated with extremely large data sets, such as whole-genome sequences or the results of large, multicenter clinical studies; such data sets can be presented more thoroughly on line than in a print journal. The greater integration of data with written text that is made possible through on-line resources should help readers better appreciate and understand research results.

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To the Editor: We are concerned about Dr. Relman's critical assessment of the E biomed proposal. Electronic information systems are radically changing the ways in which we as scientists and clinicians communicate and inform, and they have at least as much power and impact as the printing press and the telephone. To advocate the continuation of the current traditional but cumbersome system in the face of the evolving new media is, at best, short-sighted and, at worst, may signal the loss of control by physicians of the information systems on which we depend.

Electronic systems can provide the information physicians need. Publication on the Internet offers interactivity, multimedia capability, and dynamic response. Results and conclusions can be expressed with interactive spreadsheets or streaming video instead of being limited to text or still photographs. Readers can download data for additional analysis or interact directly with the author. Review panels can disseminate commentary to large, geographically diverse audiences without relying on interpretation by the media, allowing peer review to take place within a virtual community of experts and users.

We have the opportunity to develop this powerful form of technology into a scholarly tool. If we do not take the helm, its development will no doubt be directed by commercial interests. Pharmaceutical and biotechnology com-

panics with virtually unlimited resources are already using principles of marketing and advertising, rather than those of science and scholarship, to disseminate biomedical information.

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To the Editor: The balance between the timely release of data and appropriate review is always a delicate one. Dr. Relman's commentary is balanced and thoughtful. But an additional factor should be examined. The biotechnology industry, spawned less than a quarter of a century ago, has added another dimension to be considered. Today, biomedical news often influences Wall Street. There is now ample evidence that the announcement of scientific results, sometimes in advance of critical review, can cause wild gyrations of stock prices. The prestige of a "publication" sponsored by the federal government (which is naturally assumed to be unbiased), without the appropriate checks and balances, can be easily misinterpreted or, at worst, misused. The ensuing mayhem and confusion will not only reflect badly on the scientific community, but it could also make us unwitting accomplices to questionable practices.

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Dr. Relman replies:

To the Editor: I agree with Ammann that the international electronic dissemination of clinical-research reports under noncommercial sponsorship would be a good thing. As he says, "the question is, who will publish them first?" I advocate initial publication by scholarly peer-reviewed journals, with subsequent electronic posting, but he prefers initial dissemination of a "peer-reviewed site" under NIH sponsorship. The problem is that the E-biomed proposal would allow — even encourage — the posting of reports that have had no meaningful peer review and therefore would be of highly variable quality and reliability. That is an invitation to chaos.

Brodkin and Gerstein are correct that E biomed would permit the publication of far more detailed data than most print journals can accommodate, but a subsequent electronic version of a report on a journal's Web site could meet that need, particularly if the electronic version promptly followed the print publication.

Bell and Ruskin's description of how the publication of unreviewed data on the Internet (presumably on E-biomed) might be analyzed seems fanciful. Do they really think that a "virtual community of experts and users" could conduct on-line peer review that would help clinicians to interpret and use the information in their practices? That seems quite unlikely to me. Who would moderate the discussion, and how would differences of opinion and conflicting claims be resolved? The Internet contains a jumble of information — some good, some bad, and some of uncertain quality. Even with input from "experts and users" it simply could not provide practitioners with the kind of assistance they receive from the reports, reviews, and commentary found in high-quality peer-reviewed journals. Yet, E-biomed, as initially proposed, would probably threaten the survival of many good clinical journals. Some may consider that statement to be self-serving, but I believe it is nonetheless true.

Finally, I agree with Tramont about the major abuses that would attend the immediate electronic publication of unreviewed clinical reports. Nonprofit administration of the Web site and the absence of advertising would not prevent commercial exploitation of the reports, especially those sponsored by biotechnology and pharmaceutical firms. The words "mayhem and confusion" are not too strong to describe what would probably happen.

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Transplantation of Anergic Histoincompatible Bone Marrow Cells

To the Editor: Guinan et al. (June 3 issue)[1] reported an interesting method for preventing graft-versus-host disease after bone marrow transplantation. CTLA-4–Ig was added to a culture of a mixture of irradiated mononuclear cells from the recipient and marrow cells from the donor. After 36 hours, the recipient and donor cells were infused into the patient. The incidence of graft-versus-host disease after transplantation of haploidentical bone marrow (from a donor mismatched with the recipient for one HLA haplotype) was lower than expected. The authors attribute the inhibition of alloreactivity to anergy of the donor T cells, mediated by blockade of the B7:CD28 pathway.

In their study, however, high numbers of irradiated apoptotic recipient cells were injected, as indicated by the increase in the absolute number of CD3+ cells in the inoculum. Apoptotic cells induce the production of high levels of interleukin-10, which has immunosuppressive properties.[2] Furthermore, antigen-presenting cells (of donor or recipient origin) may phagocytose an excess of apoptotic cells and present recipient antigens to donor T cells in a way that induces immune tolerance.[3] To our knowledge, there are no studies of the use of recipient apoptotic cells to prevent graft-versus-host disease, but data recently obtained in our laboratory indicate that donor apoptotic cells can induce tolerance in the host. These results suggest that administration of ex vivo activated T cells or apoptotic cells, or both, with a bone marrow graft is not without immunologic consequences and could be an easy way to induce tolerance of host antigens.

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1. Guinan EC, Boussiotis VA, Neuberg D, et al. Transplantation of anergic histoincompatible bone marrow allografts. N Engl J Med 1999;340:1704-14.