leagues in the Siberian Division of the Academy of Sciences of the U.S.S.R. (*1*).

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REFERENCES

1. A. P. Derevyanko *et al.*, *New Developments in the Siberian Paleolithic: Discoveries, Facts, Hypotheses* (Univ. of Illinois Press, Champaign, IL, in press).

Orphan Drug Act

Ann Gibbon's recent article "Billion-dollar orphans: Prescription for trouble" (News & Comment, 11 May, p. 678) addresses several points about the Orphan Drug Act and proposed changes to it. However, the article missed, where erythropoietin (EPO) is concerned, the most crucial point: EPO, even under the current law, should not be an "orphan" product, nor should the act block the access of our EPO product, Marogen Sterile Powder, to the marketplace.

The matter is simple. First, orphan drug law does not supersede U.S. patent law. It is incorrect and illogical for the "orphan" status of Amgen's EPO product to deny market entry to Marogen, whose developers hold the dominant U.S. EPO patent. Second, the best available data suggest that the number of anemic kidney patients who could benefit from EPO therapy is well beyond the 200,000-patient limit for true "orphan" products. Third, the Orphan Drug Act requires that "orphan" designations and product registrations be for the same indications; Amgen's are mismatched. The Amgen product was designated an "orphan" for treating anemia associated with end-stage renal disease, which is not a separate disease state to begin with, while its product was registered to treat both anemia predialysis and dialysis patients.

All of these issues have been raised before the U.S. Food and Drug Administration in the form of a Citizen Petition filed in November 1989 and amended this past January.

Gibbons' implication that Genetics Institute, our development partner, has somehow tinkered with the Amgen molecule in order to enter the EPO market is both incorrect and unfair to scientists at Genetics Institute who carried out brilliant EPO research. The fact is that Genetics Institute alone discovered the drug form of pure, homogeneous EPO and then, in research parallel to and independent from Amgen's, successfully cloned the EPO gene. Had Amgen never conducted EPO research, Genetics Institute still would have isolated and manufactured recombinant human EPO.

The concept of the Orphan Drug Act is sound and, in most cases, the law has worked well. We think the law can be strengthened and together with Genetics Institute and The Upjohn Company, support components of Representative Henry Waxman's initiative toward that end. Gibbons suggests that Waxman's proposal could hamper development of "orphan" drugs; more likely, such changes might "dissuade" firms from trying to squeeze out monopolistic rights for products that are hardly "orphans," rights to which they should not be entitled. Our support for the Waxman amendments, however, does not alter the fact that no changes to the act are needed to make Marogen available to physicians and patients. All that is required is the correct application of the Orphan Drug Act as it now stands.

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The value of the Orphan Drug Act, particularly its 7-year marketing exclusivity provision, was touched on in quotes from a

number of people in Gibbons' 11 May article. However, the article did not contain important data critical to an understanding of the impact that the oxymoron of "shared exclusivity" would have on the development of drugs to treat rare diseases.

A recent survey by Pharmaceutical Manufacturers Association revealed that 133 orphan drugs are in human clinical tests or at the Food and Drug Administration for review. These projects involve 85 companies, including many small firms that can now afford such costly and risky research because of the act's 7-year market exclusivity provision.

The National Commission on Orphan Diseases, authorized by Congress in 1985, recognized that the market exclusivity granted by the act was critical to orphan drug research and recommended lengthening the exclusivity period.

The importance of the act's exclusivity provision was reinforced by a recent survey by the Pharmaceutical Manufacturers Association (PMA) in which member companies were asked about their current and future investments in orphan drug research and development and about the possible impact of "shared exclusivity" on their ability to continue such investments. The response from the firms that accounted for 80% of PMA members' investment in orphan drug research was that "shared exclusivity" would be sufficient reason not to pursue orphan research.

These same firms account for 91% of what PMA companies expect to spend in the future. In addition, more than one-third of the companies surveyed reported that uncertainty over the pending amendments *already* is a factor in decisions about drug research.

"Shared exclusivity" (or simultaneous development, as it is now being called) would dilute the most powerful incentive in the Orphan Drug Act and inhibit investments in rare disease research.

Gibbons' article did not mention that there are alternative approval routes for simultaneous developers. Companies may obtain designations for other indications for the same drug. The exclusivity obtained for the orphan use does not extend to other uses. Also, companies may obtain orphan designation for a similar, but structurally different, drug.

Between 10 and 20 million Americans suffer from 1 of the 5000 known rare diseases. These people are desparate for a medical breakthrough. Yet, H.R. 4638 and S. 2576 will gut the Orphan Drug Act—and their best hopes for that breakthrough.

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Billion-Dollar Zeolite?

Joseph Alper's article "Archimedes, Plato make millions for big oil!" (Research News, 8 June, p. 1190) contains the surprising statement, "ZSM-5 converts methanol into the mixture of hydrocarbons known as gasoline—a reaction of billion-dollar significance." This is nonsense on two counts. First, there is no available large, cheap supply of methanol that could be converted into gasoline. And second, if there were, the federal government would likely rule that it must be used without conversion as a motor fuel, since it burns more cleanly than gasoline.

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Erratum: In figure 2B (p. 1236) of the report "Induction of $CD4^+$ human cytolytic T cells specific for HIV-infected cells by a gp160 subunit vaccine" by R. J. Orentas *et al.* (8 June, p. 1234), the labels for HIV-infected and mock-infected cells were reversed.