terms "suitable" and "proximity" would be done with the help of the couple involved.

To get enough job openings into such a system (or to interconnect the existing systems) is likely to be a substantial effort, but the expense conceivably could be borne by affirmative action programs in public and private institutions.

This kind of help for couples in academia could be extended to other kinds of two-career households. One could simply list the locations of the jobs not by institution and institutional proximity but by zip code.

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Nuclear Accident

Peter A. Morris (Letters, 13 July, p. 148) discusses the "eminently safe nuclear operations in the United States" accomplished during the development and application of high-powered nuclear reactors. No mention is made of the SL-1 accident which occurred at the National Reactor Test Station in Idaho on 3 January 1961 (*1*). At the time, the reactor in question was managed by Combustion Engineering, Inc. This accident is notable in that the entire crew of three persons who were on duty died within hours of the event as a result of their injuries. It is important to note that the development of high-powered reactors in this country was not totally free of safety errors, as Morris' letter might suggest.

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1. W. B. Cottrell, *Nucl. Saf.* **3**, 64 (1962).

Phenacetin Studies

Macklin *et al.* (Letters, 13 July, p. 144) write that phenacetin is not as harmful as the many reports concerning its carcinogenicity would indicate. We are concerned that their letter and the previous one by Cuatrecasas (5 Jan., p. 6) may introduce a number of misconceptions into the literature if left unanswered.

The case reports concerning the carcinogenicity of analgesics containing phenacetin cannot be considered insignificant. Attention was drawn to the carcinogenic properties of phenacetin by the association of the abuse of this drug with the development of a relatively uncommon type of tumor, that of the renal pelvis. More than 140 cases of kidney and bladder tumors have now been reported in the literature (*1*) among abusers of phenacetin-containing analgesics, that is, those taking more than 1 gram per day—the maximum recommended dose of some products that are currently available in this country without a prescription. Phenacetin-containing analgesics are usually of two types: those containing antipyrine (phenazone), phenacetin, and caffeine and those containing aspirin, phenacetin, and caffeine. The mutagenicity of *amino*pyrine is irrelevant, since the patients in the Swedish studies were known to have taken primarily antipyrine-containing analgesics. Phenacetin and caffeine are the ingredients common to all the analgesic mixtures implicated in the above reports of tumor induction in Sweden, Australia, and the United States. There is no reason to believe caffeine is the causative agent.

In studies (*2*) that show evidence of phenacetin carcinogenicity, doses of 500 milligrams per kilogram or higher were administered. Human abusers of the analgesic mixtures often take 20 milligrams per kilogram per day for 20 years or more before kidney failure or tumor formation occurs. Given the fiscal and statistical limitations of experimental carcinogenesis studies, it appears reasonable to administer 500 milligrams per kilogram per day for 2 years to the relatively small numbers of animals usually employed in such tests.

Unlike the studies cited above, the Burroughs Wellcome study of phenacetin effects on C57BL/6 mice has not been published or made available to the scientific community. A single negative experiment with one inbred strain is not definitive, since the animals may have a genetically restricted capacity to carry out the metabolic events crucial to the carcinogenic process. The metabolic events responsible for the carcinogenic activity of a compound are not necessarily those that contribute to its acute toxicity.

The Data Evaluation/Risk Assessment Subgroup of the National Cancer Institute's (NCI's) Clearinghouse on Environmental Carcinogens considered the NCI bioassay (*3*) of an aspirin, phenacetin, and caffeine (APC) mixture to be inconclusive rather than negative. It was unanimously recommended by this committee that APC be considered for retesting in the bioassay program. Urinary tract and endocrine tumors were found that were considered important, al-