tion only after 1989. There is evidence also that forced labor of this sort was used in the Soviet atomic project (5), although the magnitude and extent of the practice deserve further study.

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# Contamination of cDNA Sequences in Databases

We have evidence for heavy contamination of a large data set of human complementary DNA (cDNA) sequences in the nucleotide data libraries by sequences of an unknown prokaryote. We have retrieved from the databases 4888 putatively expressed human cDNA sequences that have been deposited recently from different human genome sequencing projects and have compared them [for a description of methods, see (1)] with the latest version of the SWISS-PROT protein database. The search showed that the largest of these collections of sequences [2366 entries in the European Molecular Biology Laboratory (EMBL) database as of 5 February], representing one set of cDNA clones derived from a T lymphoblastoid cell line, is heavily contaminated by prokaryotic sequences (Table 1).

### Table 1.

cDNA library	Total se- quences	Eukary- otic-like	Prokary- otic-like
T lymphoblastoid	2366	120	278
Skeletal muscle	356	35	0
Cardiac muscle	291	81	0
Fetal and adult brain	1875	386	1

The contamination is a major one involving more than 700 kilobases of human expressed sequence tags, of which at least 83 kilobases are of nonhuman origin. The contaminated sequences will remain in the database for the next few months, characterized as "human partial cDNAs." We propose that all sequences from the contaminated cDNA library except those that are clearly of human origin be moved from the "primates" section of the databases to the "unannotated" section.

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### **References and Notes**

 The human cDNA sequences used for our search were retrieved from EMBL database release 33 and the EMBL daily updates until 5 February 1993. Sequences submitted by the Genexpress cDNA Program were selected by searching for the string GENEXPRESS in the author line (3013 entries from three cDNA libraries), and sequences from the United Kingdom/Molecular Research Council Human Genome Mapping Project were selected by searching for HSAAA as the first five characters of the entry name (1875 entries from two cDNA libraries). We used the program



BLASTX (2) to compare these sequences (translated in six frames) with the protein sequences of the SWISS-PROT database release 24 on a silicon graphics cluster. The results were processed by taking the five best "hits" of each BLASTX output and filtering them to remove those with Poisson probability [*P*(*n*)] greater than  $10^{-5}$ . A sequence showing the lowest *P*(*n*) with a eukaryotic protein was considered to be "eukaryotic-like," while a sequence with a top-matching prokaryotic protein was designated "prokaryotic-like." The complete results of this search are available by electronic mail.

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# Biotechnology in Japan

June Kinoshita, in her article "Is Japan a boon or a burden to U.S. industry's leadership?" (News, 29 Jan., p. 596), recounts a survey of Japanese pharmaceutical biotechnology that provides in some respects an update of a survey performed by the U.S. Food and Drug Administration (FDA) in 1988 (1).

Kinoshita cites a number of significant obstacles that prevent Japan from being a major competitor, but she does not mention that the regulatory climate in Japan has been, at best, equivocal toward new biotechnology. Japan has adopted a technique-based regulatory approach—with special requirements for products derived from recombinant DNA, and several areas have been significantly impeded. For example, despite a medical and scientific infrastructure that could support clinical trials of human gene therapy, no Japanese group is close to moving into the clinic, and no Japanese company has been created with gene therapy as its goal. By contrast, gene therapy trials are already under way in the United States, Italy, France, the Netherlands, and China, with almost 100 patients having been treated and the numbers rising exponentially (2).

Japan's attitude toward the new biotechnology is similarly reflected in agricultural biotechnology. Only a single field trial of a recombinant DNA-manipulated plant has been carried out in Japan (and none of microorganisms), and Japanese research and development in this area is behind what one would expect. The Japanese government has provided little encouragement in the form of clear, predictable, risk-based regulation to those contemplating field trials. Moreover, the Japanese Ministry of Health and Welfare has imposed a strict regulatory regime specific to foods and food additives manufactured with recombinant DNA techniques (3).

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# Gene Therapy Approval Process

I would like to comment on several statements in the article "Harkin seeks compassionate use of unproven treatments" (News & Comment, 11 Dec., p. 1728) by Larry Thompson regarding a request by the San Diego Regional Cancer Center (SDRCC) that the National Institutes of Health (NIH) adopt a policy to expedite the review and approval of gene therapy protocols in cases involving terminally ill patients.

The central issue, all but lost in the article, is that NIH did not at the time have in place a policy to review and act on requests by terminally ill patients seeking the benefits of new gene therapy methods (1). The request was not a means of avoiding peer review but an attempt to streamline an existing process that in some cases literally exceeded the life expectancy of the patients seeking help.

