Brundtland, a former physician and health administrator before she entered politics, said last month in Oslo that she would stand provided enough countries backed her. She will need the support of a number of developing countries, which dominate the WHO's members, if she is to succeed. One diplomat said that Brundtland, with her high political profile and track record in public health, was "a heaven-sent candidate" for the agency.

In recent years the WHO has been increasingly criticized for losing a sense of direction under its current director-general, Hiroshi Nakajima. Nakajima, elected in 1988 and re-elected in 1993 despite the unprecedented opposition of the United States and most other industrialized nations, has been criticized as a poor communicator and a weak leader under whose rule the UN agency has been unwilling to set priorities. Meanwhile other international agencies, particularly the World Bank, have increasingly taken a lead on global health.

PHYLLIDA BROWN
London

Gene therapy gets the green light in Japan

After years of deliberation and discussion, Japan is about to embark on a trial of gene therapy. The trial, approved by the Ministry of Health and Welfare's Central Pharmaceutical Affairs Council and due to start in July, is the country's first gene therapy experiment to be backed by a pharmaceutical company. According to some analysts, its most important impact will be "symbolic" — helping to build public understanding of this form of treatment.

Gene therapy has been slow to get started in Japan. Until now, there has been only one previous experiment, in 1995 — a test of a gene therapy on a boy with adenosine deaminase deficiency, which was performed for research purposes only (*Nature Medicine* **1**, 856; 1995). The new trial is planned by the Osaka-based pharmaceutical company Green Cross Corporation, Japan's leading blood products manufacturer (see page 481), and Kumamoto University Hospital, in southern Japan. It will test an immunotherapy for HIV on four people infected with the virus.

Japan has been trying to boost its gene therapy efforts. Several research groups at leading national universities in Japan are now working on developing vectors for gene therapy, but no clinical trials of domestically produced vectors have so far been conducted.

The HIV trial will use an experimental therapy developed and manufactured by Viagene, a biotechnology company based in San Diego, which has itself been bought by Chiron, another California-based company. HIV-IT(V), as the experimental therapy is known, uses a nonreplicating mouse leukemia retrovirus as a vector to deliver the genes encoding two of HIV's proteins, Env and Rev. In earlier studies in the US, this therapy has been shown to stimulate killer T cells against HIV-infected cells. Chiron and Green Cross are already conducting a phase II trial of the therapy in the USA, in about 200 people with HIV, but its clinical impact is still not known. Unusually for a Japanese pharmaceutical company, Green Cross owns the worldwide marketing rights to the protocol.

The Japanese trial, small as it is, has taken years to achieve. Clinical trials of HIV-IT(V) began in the United States in 1993. Doctors at Kumamoto University first approached their university ethics committee in late 1994 to seek approval for similar trials in Japan on behalf of Green Cross. But they then had to wait for official safety guidelines to be drawn up (*Nature Medicine* **1**, 233; 1995) and for committees at two ministries to approve the trial.

The treatment prospects for people infected with HIV have changed considerably in the three years since the doctors first sought approval for the trial. New approaches for treating HIV using combined drug cocktails and protease inhibitors have proved promising in early trials. In the USA, Chiron and Green Cross have expanded their trial to test the gene therapy in combination with new protease inhibitors. None of the four patients who plan to participate in the Japanese trial currently take these drugs. Indeed, only one protease inhibitor has so far been approved in Japan. However, the patients are currently taking a combination of three other antivirals, zidovudine (AZT), didanusine (ddI) and (–)2',3'-dideoxy-3'thiacytidine (3TC), and doctors at the university do not rule out the possibility that they will start taking protease inhibitors in future.

Nonetheless, some experts in Japan argue that new advances in drug treatment for HIV make the gene therapy approach redundant. Other industry experts point out, however, that HIV may build up resistance to these new treatments and it is essential to explore all possibilities.

Takahisa Murakami, an official at the Ministry of Health and Welfare, sees no problem with proceeding with a trial, provided the doctors seek "sufficient" informed consent from the participants. The consent documents for the trial are now being revised to ensure that patients know about alternative treatments.

Because the Japanese trial is so small, it will be extremely difficult to obtain scientifically meaningful results from it. Murakami says the trial "is not essential for Japan." But doctors counter that it is their job to offer patients a choice of treatment.

RICHARD NATHAN
Tokyo