AIDS activists seek speedy access to protease drugs...

Washington. Attempting to tackle one of the thorniest issues posed by the newest class of antiviral AIDS drugs, namely protease inhibitors, the US National Task Force on AIDS Drug Development last week set up a group to decide who should qualify for compassionate use of the drugs while they are undergoing the approvals process.

Three companies — Roche, Merck and Abbott — have protease inhibitors undergoing human trials. Encouraged by promising experimental results and the fact that these drugs seem to have fewer unpleasant side effects, AIDS patients are pressing the companies to apply for accelerated approval as soon as possible. This is available for drugs that treat life-threatening diseases, and the three companies could be ready to apply towards the end of the year.

While the approvals process goes ahead, AIDS activists argued last week (as they have done in previous cases) for concurrent programmes of expanded access for compassionate use. Expanded access programmes exist in a variety of bureaucratic guises, but all have the same aim: to provide treatment for people who have no other medical option in the period just before a new therapy gains approval. The term "salvage therapy" used by AIDS activists says it although Philip Lee, an Assistant Secretary for Health and head of the task force said that he would prefer them to talk of life-sustaining therapies.

Expanded access is always a difficult issue, but it is amplified in the case of protease inhibitors. This class of compounds has a complex structure that the companies say is particularly difficult to manufacture. All three are increasing production, but yields are low. Abbott, for example, is getting yields as low as two per cent.

To compound the difficulty, each patient needs about 1 kg of the drug a year, which is "50 to 100 times as much as other antiviral drugs", says Edward Scolnick, president of the Merck Research Laboratories and a member of the task force. So the question to be answered is how should the limited supply of drugs available be divided between expanded access programmes and clinical trials aimed at gathering the data necessary for accelerated approval?

Although there was no formal vote, the consensus from both panel and advocates in the audience was that the trials needed for approval should take precedence, thus leaving smaller quantities of the drug for expanded access, and creating the need for a group to make tough decisions about who should receive what little is available.

Roche, which is the furthest ahead in its development work and has already agreed to supply 4,000 people with its protease inhibitor through expanded access, welcomed the decision. "We don't like playing God," said a spokesman for Roche, "so if decisions can be made jointly, we'd be happier." Merck, has so far agreed to provide drugs to 150 people, and Abbott, the newcomer, is still discussing with AIDS advocates what it will supply.

One proposal supported by AIDS activists both on the task force and in the audience was that the Food and Drug Administration (FDA) should have regulations requiring companies applying for accelerated approval to have an expanded access programme in place. And those regulations should provide guidelines for the nature of the expanded access programme, "We don't want to spend months negotiating every time there is a new drug," said Jules Levin, an advocate from San Francisco who represents people with CD4 counts lower than 200.

Expanded access, however, poses problems for industry. The company cannot make a profit on drugs supplied through expanded access (they are not approved). They can recover their costs, but with difficulty. And there are other problems. Although the FDA must agree to a drug being available through expanded access programmes, there is a legal risk ing supplying a drug that is not fully approved and which is backed by incomplete safety data.

Stephen Carter, senior vice president for worldwide clinical research and development at Bristol-Myers Squibb (manufacturers of a different class of antiviral , ddI), said after the meeting: "We spent a lot of money when ddI was released on expanded access, and we were very nervous. We were moving on data from only 92 patients."

Helen Gavaghan

UK signs agreement with South Africa on joint projects

Cape Town. An 'enabling' agreement to collaborate on joint scientific projects was signed in Cape Town this week by David Hunt, Britain's science minister, and his South African counterpart, Ben Ngubane, Minister for Arts, Culture, Science and Technology.

Under the agreement, a joint committee will be set up to advise the two governments on how collaboration can best be achieved. Both South Africa and Britain will contribute £100,000 each for three years to a new fund established to support joint scientific research projects.

Further contributions to the fund are being sought from the private sector. In addition, a medal worth £10,000 will be awarded for the best collaborative project between researchers in the two countries.

During a visit designed to follow up an initiative launched by John Major, the British Prime Minister, during a visit last September. Hunt attended colloquia on agricultural research at the University of Stellenbosch, and on science and the environment, at the Council for Scientific and Industrial Research in Pretoria. He handed over equipment to the South African Astronomical Observatory at Sutherland in line with an agreement with the UK Particle Physics and Astronomy Research Council.

Conspicuously absent from the proceedings was Mrs Winnie Mandela, South Africa's Deputy Minister of Arts, Culture, Science and Technology, who is attending a film festival in Burkina Faso. Mrs Mandela defied orders from Nelson Mandela, President of South Africa and her estranged husband, to remain in South Africa and meet her commitments. It is widely expected that he intends to dismiss her when she returns on 6 March.

Michael Cherry

...as companies plan combination trials

Washington. The so-called 'Inter Company Collaboration' of US pharmaceutical companies this week begins the first of a series of small clinical trials designed to evaluate the relative effectiveness of different combinations of antiviral drugs against AIDS.

Initially, the trials will include only combinations of the AZT types of antivirals, but as protease inhibitors work their way down the pipeline, these too will be added to the combination trials.

But the design of these and other types of clinical studies drew criticism last week from AIDS activists, concerned that the kind of information that they are seeking cannot be extracted from the trials as currently designed.

The criticisms, expressed at a meeting of the National Task Force on AIDS Drug Development (see above) prompted an irritated response from Edward Scolnick, president of the Merck Research Laboratories and a member of the task force. "Merck does know how to design clinical trials," he retorted at one point.

But David Kessler, commissioner of the Food and Drug Administration, agreed to back a workshop looking at the design of clinical trials. This will be organized by Peter Stayley, a task force member from the Treatment Action Group in New York and David Fiegel, director of FDA's division of antiviral products. **H.G.**