'Better adherence vital in AIDS therapies'

[WASHINGTON] Combination therapies for HIV-positive patients will not help certain high-risk groups unless researchers can rapidly improve their ability to persuade patients to follow the complex drug regimens involved, a meeting in Washington DC was told last week.

The Forum for Collaborative AIDS Research, a public–private-sector partnership group which helped to organize the meeting, is to prepare a 'research agenda' for the US National Institutes of Health (NIH) and drug companies, proposing ways in which biomedical and behavioural scientists can cooperate to achieve that goal.

Gerald Friedland, head of the AIDS programme at Yale University School of Medicine and co-chair of the meeting, described patient adherence as "perhaps the greatest challenge" to combination therapies. "Adherence has now emerged as the Achilles' heel" of such therapies, he said; improving it would be "a daunting task".

Since early 1996, when researchers established that aggressive treatment with combinations of antiretroviral drugs could successfully suppress HIV levels and thus prevent the onset of full-blown AIDS, the therapies have been widely prescribed in the United States. As a result, the number of new AIDS cases has already fallen sharply.

But the therapies require patients to follow arduous regimens, taking up to ten pills a day at fixed times. Data from clinical trials indicate that a treatment's effectiveness can be permanently undermined by even brief non-adherence. Failure to take the drugs at the right times, even for a few days, can lead to restoration of the viral load to previous levels — and with a virus resistant to the therapy being used.

Scientists and advocacy groups also fear that such non-adherence might generate HIV strains resistant to all available combination therapies. But data on such an outcome are sparse. The question "isn't being looked at systematically", says Friedland. "We don't yet know if such resistant strains will emerge," he says, "but nothing indicates that it will not happen."

The meeting, co-sponsored by the National Minority AIDS Council and NIH's Office of AIDS Research (OAR), heard that existing knowledge on patient adherence was of little help to AIDS researchers. Most therapies are insensitive to minor lapses, so ensuring strict adherence has been a low research priority.

The research agenda, to be published early next year, is likely to suggest research work in three main areas of interest, officials at the Forum and at OAR said: techniques for measuring patient adherence, factors that predict patient behaviour and interventions to change that behaviour.

Options for measuring adherence include technology-based solutions, such as drug-bottle caps that electronically record whenever the bottle is opened, as well as self-reporting by the patient, although this is known to have flaws.

Although it is sometimes assumed that the high-risk groups now being targeted for combination therapies, including drug addicts and homeless people, will not adhere to complex drug therapies, this assumption is not well supported by existing data, and more research is needed to identify the factors that influence adherence.

Interventions to encourage adherence can range from education and family support to cash incentives, which have been tested with some success on homeless people in San Francisco. But again, the meeting heard, little is known about which approaches are most effective.

As well as identifying necessary research in the three areas, the research agenda will prioritize the activities as immediate, medium-term and long-term, and suggest which government agencies or drug companies are best placed to pursue each one.

Officials at the Office of AIDS Research, which coordinates the $1.5 billion AIDS research programme at NIH, pledged to follow through on the research agenda. "We did a poll across the NIH institutes in the summer to see what they were doing about adherence and we discovered there is still not very much going on," says Judith Auerbach, chair of OAR's behavioural and social science coordinating committee.

Work to study patient adherence is already under way at several NIH institutes and more is being supported by OAR's new $7-million-a-year Prevention Science Initiative, Auerbach says.

The urgency of investigating adherence has been raised by recently published studies indicating that combination therapies will never eliminate the virus, so that patients must stay on the complicated therapies indefinitely to prevent the onset of AIDS.

Some speakers at the meeting questioned whether patients could ever adhere to such complex therapies. "Imperfect adherence is a medical fact of life that should be accepted," said Charles Flexner, a pharmacologist at Johns Hopkins University Medical School in Baltimore, Maryland. Flexner predicted that better drugs, with far simpler regimens, will become available within two years.

"I have no doubt that we'll see more friendly drug regimens in a couple of years," says Tony Fauci, director of the National Institute for Allergy and Infectious Diseases, the NIH institute that supports most AIDS research. "But that doesn't rule out the need to understand adherence, or the lack of it, in individuals."

William Paul, director of the Office of AIDS Research until his return to research at the end of last week, says that more research into adherence "would be a small cost and, if we can make some headway it might be very valuable".

Colin Macilwain

Sub-Saharan Africa hit hardest by epidemic

[WASHINGTON] While the United States works to contain AIDS with sophisticated combination therapies (see above), developing countries are being ravaged by the epidemic more rapidly than ever, according to the United Nations AIDS programme (UNAIDS).

According to UNAIDS' annual survey, released this week, 5.8 million people were infected with HIV this year, while the total number of adults infected was just under 30 million – one in a hundred of the world's adult population.

The epidemic remains overwhelmingly centred on sub-Saharan Africa. UNAIDS has revised its previous estimates for the region sharply upwards by using new models that take into account the differing pattern of the epidemic in different countries.

UNAIDS: HIV cases up again.

"The more we know about the AIDS epidemic, the worse it appears to be," says Peter Piot, executive director of UNAIDS. "In sub-Saharan Africa, the situation is even more desperate than had been thought." More than 20 million people, or 7 per cent of the adult population, are now infected with HIV in sub-Saharan Africa, UNAIDS says. Worldwide, 2.3 million people will die of AIDS this year.

UNAIDS has also revised upwards the estimates it published last year: after the adjustment is taken into account, the number of new infections rose 9 per cent this year from last, and the total number of people infected with HIV grew by 13 per cent.

After sub-Saharan Africa, south/southeast Asia has the highest number of people infected with HIV, according to UNAIDS, at 6 million. Latin America comes next, with 1.3 million people infected. The figure for North America is 860,000 people, and for western Europe 150,000 people. **C.M.**