# Row over controversial new AIDS drug

## ■ Doctors enraged by *ad hoc* trial
## ■ Benefits claimed by patients

***San Francisco***

A HIGHLY controversial 'clandestine' study indicates that the promising AIDS drug Compound Q is not the cure many had hoped but, rather, one potentially useful — but extremely toxic — weapon in the growing arsenal being brought to bear against the disease.

The San Francisco advocacy group Project Inform established the trial last May after *in vitro* studies showed that Compound Q selectively killed cells infected with HIV, the virus causing AIDS. Organizers argued that patients had already begun to taking the drug on their own initiative and that federal safety and efficacy trials were proceeding too slowly. The *ad hoc* trial outraged many doctors and researchers, who felt that it undermined traditional science. And last week's announcement of the first results further emphasized the split over the issue.

Project Inform co-director Martin Delaney received a standing ovation when he proclaimed at a public meeting: "We have reported faster over this protocol than any research in the history of the epidemic". But Professor Jerome Groopman of Harvard Medical School condemned the effort. "This is an important and a very bad precedent", he said. "This is not the way we are going to identify effective treatments for AIDS." The trial's most conclusive data concerned the toxicity of the drug, which is derived from a cucumber-like plant and which has been used in China to treat cancer and induce abortions. Almost all the 51 patients in San Francisco, New York and Florida developed side-effects, ranging from fever and rash to violent dreams and coma. Three patients died after taking Compound Q, but researchers said all were in advanced stages of the disease and that no direct relationship could be established between their deaths and the drug.

On the positive side, many patients showed signs of benefiting from Compound Q. The Florida group was dropped from all except the toxicity data because doctors there used a wide range of dosages and administration methods that made comparisons impractical. But the 34 patients in San Francisco and New York generally showed an increase in the count of CD4 cells, which are depleted by HIV infection. Researchers were encouraged by several other findings. One involved P24 antigens, high levels of which are typically associated with an advanced stage of AIDS. Results of this test were announced only for the 19 San Francisco patients: 15 showed a decline and nine showed a sustained drop averaging 50 per cent. In addition, 12 of the San Francisco patients reported feeling more energetic than they had in months.

Nine gained weight and seven said they were mentally sharper. While trial organizers stressed that Compound Q is not a cure for AIDS, they insisted that it shows promise — especially if used with other drugs, such as AZT, which interfere with HIV's ability to infect new cells. Dr Alan Levin, who helped to organize the trial, said, "I believe that in combination with other drugs it has the potential for cure". Soon after the trial became public, the US Food and Drug Administration (FDA) launched an investigation, which is still continuing. Delaney claims that the trial is legal because it was established as a "treatment protocol" between doctors and existing patients, rather than a clinical study. Nevertheless, Project Inform took elaborate precautions to warn patients of the risks involved, both to assuage FDA fears and to avoid lawsuits.

A lawyer and a patient advocate were on hand as each subject signed the informed consent agreement — and the entire process was videotaped.

But opponents were unconvinced. "Martin Delaney and Al Levin are not competent to do experimental drug trials", said Groopman, who said he supports community-based research but not when it involves a highly toxic drug used for the first time in humans against a particular disease. He added: "It's quite likely patients unnecessarily suffered". Groopman attacked the trial on other grounds, challenging the protocol and criticizing the absence of a neutral third-party review. Delaney said trial results will be independently evaluated. But, in general, project organizers took a hard line with critics. Levin noted that patients often experience severe side-effects during FDA-approved trials. The difference, he said, is that the Compound Q results were quickly made public.

Besides, community physicians know best what is good for their patients, "Academic physicians are not qualified to care for the chronically ill", he added.

While the debate is yet to be resolved, more traditional work continues. An FDA-approved Phase I trial of Compound Q began in May at San Francisco General Hospital. And the National Institute of Allergy and Infectious Disease (NIAID) will soon announce funding awards under its new Community Program for Clinical Research in AIDS, designed to bolster community involvement in research. Said Daniel Hoth, director of NIAID's Division of AIDS, "Our view is that there's enormous energy and enthusiasm among community physicians to do clinical trials, and we want to help them channel that to productive research that can help find out which drugs work and which don't".

**Robert Buderi**

RADIOCARBON LABORATORIES

# Blind dating exposes UK weakness

*London*

**BRITAIN'S radiocarbon-dating laboratories are to launch an international project to try to overcome a lack of consistency in their results. A workshop held at the National Engineering Laboratory (NEL) in Kilbride, Scotland, heard last week that a comparison of 40 radiocarbon-dating laboratories in Britain found a disturbing pattern of errors.**

**Three Scottish laboratories, the Statistics Department of the University of Glasgow, the Natural Environment Research Council (NERC) Radiocarbon Laboratory in East Kilbride and the Scottish Universities Research and Reactor Centre, had collaborated to design, execute and interpret a "blind intercomparison exercise" supported by the Science and Engineering Research Council (SERC).**

**In the trials, 38 laboratories were asked to date samples of wood, peat and carbonate. Professor Murdoch Baxter of NEL said the results were "gloomy". He said that only seven out of 38 laboratories had met the three desired performance criteria — negligible bias, high internal precision and negligible external variation. Radiocarbon dates were "two to three times less accurate than implied by their error terms". He said most laboratories produced differing dates when they analysed similar objects of the same age.**

**Baxter said that although delegates were "disappointed" by the results, there was a "positive determination to work together and improve the situation" and the carbon-dating community "would adopt quality assurance principles and practice". Each laboratory will improve monitoring and build up a "record of regular essays of in-house and externally supplied reference standard materials". The International Atomic Energy Authority will supply samples of wood, sediment and carbonate on request from 1990 with given dates to provide reference materials. "There are a lot of good laboratories and a lot of poor ones", Baxter said. "It is important there is more cooperation to allow the good laboratories to help the others." To monitor improvements, a second blind check will be carried out in two years with the help of the NERC.**

Ben Webb