

Dutch cure for AIDS is discredited

- Faulty synthesis an "honest mistake"
- Eindhoven chemists at odds

The Hague

THE Netherlands research community has been set on its ears by an acrimonious scandal over the intended retraction of a paper from the Eindhoven Technical University, the exclusion of its principal author, Professor Henk M. Buck, from the chemistry faculty of which he was previously the dean and demands by the elected University Council for the resignation of the rector of the university, Professor M. Tels.

The disputed research report, published in April in the US journal *Science*, outlined a possible means of interrupting the replication of HIV in cases of human AIDS (*Science* 248, 208; 13 April 1990). The scheme, described as having been effective in *in vitro* trials, rested on the synthesis of oligonucleotides complementary to DNA in naturally occurring virus, but differing from natural DNA by the methylation of the phosphate group in each nucleotide.

It is now acknowledged by Buck and his colleagues that the synthetic route developed at Eindhoven for the construction of the methylated oligomers does not yield the products expected from it, and that the materials used in the *in vitro* trials contained little or none of the 20-nucleotide methylated oligomer supposedly designed to be complementary to crucial sequences of HIV.

While the organic chemistry in the collaborative research programme was carried out at Eindhoven, the biological assay of the synthesized material was the responsibility of Professor Jaap Goudsmit and two colleagues, human retrovirologists at AMC, Amsterdam.

Controversy began with the publication of the controversial paper last April, and appears to have been stimulated by a television broadcast on the same day in which Buck was shown walking his dog in the woods, and when claims were put forward that oligonucleotides methylated on the phosphate group would prove to be a means of halting AIDS infection.

Colleagues of Buck at Eindhoven, including one co-author of the article, Dr Leo H. Koole, then protested within the university that the claims were exaggerated and that the material used in the trials had not been fully characterized chemically.

A three-man investigating committee set up within the Faculty of Chemistry to investigate the allegations reached the conclusion, using HPLC and NMR mea-

surements, that they were correct. The committee's report to the rector also stated that Buck had been warned by his junior colleagues at Eindhoven that the materials used in the research had not been fully characterized, but that expressions of doubt had been brushed aside.

The internal report also said that Buck had been dictatorial in his management of the chemistry faculty, and that research other than that disputed might have been flawed by over-definite interpretation. On 30 August, the university said in a public statement that Buck's appointment as dean had been terminated. The decision that he should also cease to be head of the organic chemistry department was decided by a vote of his colleagues.

Speaking from his home earlier this week, Buck (who is 61) said that he considered the outcome of the investigation to have been unfair. While not disputing the technical conclusions of the three-man committee about the material synthesized at Eindhoven, he insisted that until then he had had no reason to suspect that the synthetic method would yield products other than those intended. "I was convinced about everything."

Buck also says that the method has been shown to yield the expected results when there are fewer than 10 nucleotides in an oligomer. What seems to have gone wrong is that a protective group used to shield reactive nucleotide sites behaves aberrantly when larger oligomers are synthesized.

On the charge that he had overridden scepticism of his work expressed by colleagues, Buck says that no colleague ever told him openly that the synthesis used was flawed. He says that only 25 per cent of his research time was taken up with phosphate methylation, and that his more than 300 published research articles showed that he had an important contribution still to make to organic chemistry. While acknowledging that the disputed research was in error, he believes he has been pilloried for making an honest mistake.

By coincidence, Buck and his immediate colleagues had made a careful presentation of the now-disputed research to this reporter, on a visit to Eindhoven early last November. At that stage, one member of the group was asked to display four test-tubes, each containing about 10 grams of a white substance, which were said to contain phosphate-methylated DNA oligomer tailored to the viral sequences of four identified AIDS

SOVIET ACCIDENT

Under a cloud

London & Washington

NEWS emerged last week of an explosion and fire at a metallurgical factory near Ust-Kamenogorsk in Soviet Kazakhstan, near the Chinese border, on 12 September, which is believed to have released a cloud of toxic beryllium oxide into the atmosphere. Local environment protection officers say that 120,000 people may have been exposed. Early reports suggested that the explosion had taken place at a nuclear facility but the International Atomic Energy Authority says the plant is not involved with nuclear fuel processing. Rather, it appears the plant was manufacturing beryllium for use in the nuclear industry.

It is not clear whether the industry is civilian or military. Beryllium can be used around nuclear reactor fuel rods to reflect neutrons back into the reactor core, but it is toxic and very difficult to work with. Other materials that are safer and easier to use are preferred for reactor use in the West, but beryllium is still used as a neutron mirror in nuclear weapons. It is processed in the United States at the Department of Energy Rocky Plate plant.

The beryllium oxide cloud is likely to have fallen to the ground quickly and over a relatively small area. The material causes fibrosis of the lungs and may also be a carcinogen. The local government has asked that the area be declared an ecological disaster zone but no details of the impact of the accident have been released.

Peter Aldhous & Alun Anderson

patients from Amsterdam.

Buck then also announced that a paper describing the findings had been sent to *Science*, where it was received on 10 October last. He now says that in the six months before publication, the journal had raised questions about the virology, but not about the organic chemistry.

The effects of this affair on the chemistry faculty and even the university have plainly been traumatic. Several members of the chemistry staff have left for posts elsewhere. One of those remaining says the past few months have been "like living in an unreal world", and that only now does he feel that "my two legs are coming back to the ground".

Wider issues have been raised in the University Council, some members of which hold that the university rector and his colleagues must shoulder the blame for having allowed Buck allegedly to tyrannize his academic colleagues. A particular concern that seems especially to have exercised council members is that Buck deprived a former colleague of research space, thus forcing him elsewhere.

The rector, Professor Tels, was not in Eindhoven earlier this week.

John Maddox