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BRITISH PLASMA-DERIVED VACCINE AGAINST HEPATITIS B

The Issue

1. For some years the DHSS has been making a contribution - £167,000 to date - towards the development of a plasma-derived vaccine against hepatitis B, based on a micelling technique elaborated by
at the London School of Hygiene and Tropical Medicine. Doubts have been raised now about the project, triggered by difficulties with the inactivation processes necessary to render any such vaccine non-infective from free virus and by recent concern over the possibility of transmission of AIDS (Acquired Immune Deficiency Syndrome) via the human plasma from which the vaccine is derived. We need to consider whether to continue DHSS involvement either with this project specifically, or with any other use of micelling technique.

Recommendation

2. As a first step, it is recommended that Ministers agree to the commissioning of a independent and confidential scientific review of the hepatitis B vaccine work at the London School, with a view to assessing the efficacy of the technique elaborated by
. It is envisaged that the review could be undertaken by two leading scientists under the oversight of the

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Director of the National Institute of Biological Standards and Control.

The Background

3. Scientific: The basis of any hepatitis B vaccine is the surface antigen of the hepatitis B virus, which is contained in the outer coat of the virus itself. If injected into the human body, this antigen stimulates the production of antibodies by the recipient, which in turn provides immunity from the disease. In plasma-derived vaccines the antigen is obtained from the blood of chronic carriers, a small proportion of whom may still have active hepatitis B virus in the blood. Because of the risk that the extraction of antigen from carrier plasma may include some free active hepatitis B virus as well, it is essential that the production process should include operations to inactivate any free virus to obviate any risk to vaccine recipients. The Merck Sharpe & Dohme (MSD) vaccine from the United States, licensed for the United Kingdom in 1982 and now in use here, employs three such inactivation operations.

4. The MSD vaccine from the US consists of surface antigen purified from the plasma of carriers and inactivated. The British project to which this submission refers, is a variant of the other process, in that it is attempting the isolation by fractionation methods (separating constituents elements using their different physical characteristics) of purified antigenic polypeptide components of surface antigen from carrier plasma, and their possible synthesis in the test-tube. As this process also starts with the blood of chronic carriers, effective inactivation operations are equally vital if the ultimate product is to be licensed for human use.

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5. Historical: In February 1971, the London School of Hygiene and Tropical Medicine sought financial support from the DHSS for diagnostic, reference and development activities concerning testing for hepatitis A and B which was already providing as a help to the Blood Transfusion Service and various National Health Service hospitals. Extra finances were needed and the Department's then Research Division started to fund this work on a two yearly basis. This continued from 1 April 1971 to 30 April 1981 by which time a total £1370,000 had been provided.

6. By June 1979, when the administration of the project was brought more closely under the control of the Office of the Chief Scientist, the work comprised research, service and development components; the principal, although not exclusive, component being research on hepatitis B vaccines. In August 1980, was told that extension of funding beyond March 1981 would have to be subject to formal scientific assessment of any further proposals. He responded by suggesting: (1) continuation of "the development of a British hepatitis B polypeptide micelle vaccine" (and the exploration of other sources of surface antigen); and, (ii) continuation of the "work improving reference and service functions to the Blood Transfusion Service and the NHS".

7. The Professor's proposals were submitted to three referees:

(the Director of the Public Health Laboratory Service, and previously Professor of Microbiology at St Mary's Hospital Medical School), (Consultant Virologist in Birmingham), and (Consultant Virologist in South Manchester). In the light of their observations, it was agreed to provide a contribution to the funds necessary for this work, commencing on

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high risk groups to which it might be offered - the Minister for Health stressed that our positive policy must be to press on to produce a British product at a more realistic price. This has guided officials in their discussions with those working on the product, and with the Group.

11. However, in recent weeks it has become increasingly clear that the inactivation operations (explained earlier), which had not been perfected fully before starting the transfer of the technology from the London School to the Centre for Applied Microbiology & Research, was giving more trouble than had been anticipated. It is estimated now that the perfection of these operations may take at least a further year.

12. Meanwhile, the transfer of the technology to the Centre from the London School has not proceeded as well as was expected. Not only is it taking more time than had been anticipated originally for this phase, but the Centre in its own work has not been able yet to replicate the encouraging results on the efficacy of the vaccine in animal tests that had been achieved originally by the London School. These several difficulties taken together have raised questions, firstly about the technique itself, and secondly about the timing of the transfer of the technology: was it undertaken too soon?

13. On the commercial side, the Group recently has informed the researchers and the DHSS that it can find no British company, nor any foreign company with a UK base, wishing to embark on the commercial exploitation of a plasma-derived vaccine. This is due to concern which has arisen about the possible transmission

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of AIDS (Acquired Immune Deficiency Syndrome) in plasma-derived products, in circumstances where the blood donors likely to be the most productive sources of hepatitis B surface antigen happen often to be individuals at risk of developing AIDS. (Of the thirteen chronic carriers who are providing plasma for this product through the North London Blood Transfusion Centre, ten are known to be homosexuals, and thought to be in the AIDS 'at risk' group.) This concern could not have been foreseen in the earlier stages of the present project, because the origins, causes and natural history of AIDS has emerged only recently. The commercial firms have indicated that they would prefer to await the development of a non-plasma-derived product, that is one produced by genetic engineering.

14. Very recent reports have revealed that a team of microbiologists in the Netherlands have developed a hepatitis B vaccine using advanced genetic engineering techniques developed by the Molecular Biology Department at the University of Edinburgh. The reports suggest that this vaccine is likely to be available commercially in 1985, and could possibly be cheaper than any of the existing commercially available plasma-derived vaccines. (France and the Netherlands have their own plasma-derived vaccines not licensed for use in the UK, in addition to the MSD vaccine from the USA.) It is impossible to say how accurate are these estimates of availability and relative cost for the Dutch genetically engineered product.

15. Another aspect of the story, is that of Houston, Texas is adapting technique and attempting to produce his own version of the British variant, with financial support from MSD itself. The Swedes also appear to be working on an adaptation of the technique.

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16. Although there is no commercial interest in the British project at present, if it can be carried to the point of clinical trial of the vaccine - which could only follow confirmation of the earlier optimistic animal trial results and perfection of the necessary inactivation operations - it is possible that British commercial interest might then be stimulated. Alternatively, the Centre for Applied Microbiology & Research might be persuaded to manufacture a limited quantity of a British plasma-derived vaccine for use in this country. Unfortunately, on the information available at present it is impossible to estimate the likely unit cost of a product in either of these circumstances.

17. In any event, the technique elaborated by might have other practical applications if the current problems could be overcome. The question is: given the complicated background, should the DHSS continue to provide funds for the development of the technique, either as the basis of a British plasma-derived hepatitis B vaccine or for some other practical application? If so, what limitations should the DHSS apply to the provision of funds? At present, meaningful answers to these questions are impossible in the absence of up-to-date scientific assessments of the efficacy of the technique underlying the product, together with more information about the problems surrounding the transfer of the technology to the Centre from the London School. To cover the first need, Ministers are invited to commission an independent scientific review of the work at the London School, to be overseen by _____, Director of the National Institute for Biological Standards & Control (NIBSC) and Chairman of the MRC/Health Departments/PHLS Committee on the Development of Vaccines & Immunisation Procedures. (Although it is thought unlikely that _____ will be able to spare the time necessary to undertake the detail of the review itself, it is hoped he will agree

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to oversee this important and delicate exercise, for which his scientific background and standing are impeccable.)

18. It is proposed that the detailed work on the review be entrusted to [redacted], Director of the Viral Products Division at NIBSC and Chairman of the Hepatitis Vaccines Sub-Committee, together with [redacted], Consultant Virologist at the Regional Virus Laboratory, Birmingham] or [redacted], lately a Senior Medical Officer dealing with immunisation products in the Medicines Division of the DHSS]. (Pending approval by Ministers of the proposed review, no approach no approach has been made yet to any of those nominated for participation

19. In the meantime, the Director of the Public Health Laboratory Service has been asked to report in confidence on the problems experienced by the Centre for Applied Microbiology & Research in the transfer of the technology from the London School, and to offer his own appreciation of the future for the project from his Services' point of view.

Date

Deputy Chief Medical Officer

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