

EXECUTIVE SUMMARY

ENGLAND AND WALES SELF-SUFFICIENCY IN BLOOD PRODUCTS: A CHRONOLOGY FROM 1973 to 1991

The Government pursued the goal of self-sufficiency in factor VIII during the 1970s and most of the 1980s, in line with WHO and EC recommendations. The primary aim of this goal was to reduce the reliance on expensive imported concentrate, although there is some evidence that there were also concerns over the possible threat to the volunteered-based donor system in England & Wales should commercial firms decide to establish paid donor panels in this country. In the late 1970s and early 1980s, these concerns were accompanied by fears of the risk of transmission of both hepatitis and HIV infection from imported factor VIII concentrate.

In 1975, the Government allocated £0.5m, about half of which was recurring, to the NHS in order to increase plasma production. At the time, this amount was predicted to allow the UK to become self-sufficient in factor VIII by 1977. However, the demand for factor VIII in the UK increased dramatically in the late 1970s with changes to the dosage regimen for the home treatment of haemophilia. The demand was also expected to increase further as a result of longer life expectancy of patients with haemophilia, increased provision of home therapy, and the use of factor VIII in prophylaxis. Therefore, despite the increase in plasma collection and factor VIII production, the UK still relied on imported factor concentrates.

With the development of tests for hepatitis A and B in the 1970s, it became clear that non A non B hepatitis (NANBH) could be transmitted by blood. In the early 1980s, growing concerns over the safety of commercial concentrates imported from the US reinforced the need for self-sufficiency, the development of both an appropriate screening assay for NANBH and an effective viral inactivation treatment at BPL. In the meantime, the Haemophilia Society appealed to the Government not to ban American blood supplies and advised their members not to stop treatment in response to concerns over potential risks. Furthermore, doctors treating patients with haemophilia were, we believe, careful in explaining the risk of viral infection to their patients. Before 1989, potential blood donors could only be screened for NANBH using surrogate tests; however, these were perceived to be crude and inappropriate for use in the UK. With the cloning of a portion of the virus in 1989, the C100-3 antibody test became available. This was associated with a large number of falsely positive and negative results and, once again, was not approved for use in the UK. It was only in 1991 that a number of validated second-generation assays became widely available and routinely used to screen potential blood donors for NANBH infectivity.

The prevailing medical opinion in the 1970s and the early 1980s was that NANBH was mild and often asymptomatic. Research into NANBH was hindered by the lack of a definitive serological assay, the reluctance of clinicians to perform liver biopsies in patients with a very high risk of bleeding, and the fact that, in the majority of patients, the chronic sequelae of NANBH only became apparent after more than a decade. Even in the mid-1980s, however, when it became apparent that NANBH was associated with long-term chronic sequelae, including liver failure, cirrhosis, and hepatocellular carcinoma, clinicians were still advised to continue using the

concentrates. The improvement in QoL and dangers of bleeding were seen to outweigh the potential risks of treatment.

Attempts to develop viral inactivation processes to treat blood products began in the early 1980s. Available techniques resulted in a substantial loss in yield and were not capable of producing sufficient quantities of concentrates for the UK market. In 1982–1983, further products were introduced; however, their viral safety was not been firmly established and, in fact, they were later shown to still transmit NANBH. In 1985, BPL developed a new, high purity product, designated 8Y, which was capable of maintaining satisfactory yield from fresh frozen plasma, had remarkable *in vitro* stability to heat in the absence of conventional stabilisers, and had a good record of safety in clinical trials. To date, 8Y has proved safe and has not been reported to transmit hepatitis or HIV.

The decision to redevelop BPL followed an adverse Medicines Inspectorate report in 1979, and the realisation that the existing laboratory did not have the capacity to provide enough material for self-sufficiency. The redevelopment project comprised two stages: the upgrading of the current facilities at BPL over a period of 3–4 years; and the development of a new laboratory with an increased capacity. £1.3m was assigned to the short-term development at BPL and £21m to the building of a new fractionation facility. In the early 1980s, the total cost of BPL redevelopment escalated; however, the project remained fully funded owing to the Government's commitment to self-sufficiency. Furthermore, the scheme was projected to pay for itself within 5–6 years of reaching full production.

Efficient operation of the unit required 3 times as much plasma as it was currently processing, and RTCs were held responsible to meet this increased demand. Over the following years, RTCs struggled to provide the necessary amounts of plasma to BPL. By 1993, however, England & Wales produced 75% of the total requirement for factor VIII, but was still therefore still reliant on a certain amount of commercial factor VIII. This situation reflected a preference of some physicians to use commercial products over the BPL product. The Department was keen not to restrict the prescribing habits of clinicians. Furthermore, it was also felt by groups representing patients with haemophilia that there were dangers in absolute self-sufficiency. This, they claimed, would lead to a reliance on a sole supplier of blood products, which was predicted to override clinical freedom, stifle new developments (many of which were from the commercial sector), and expose England & Wales to the possibility of inadequate volumes of product for effective treatment.

Therefore, about 3000 patients with haemophilia treated with blood products in the 1970s and early 1980s were infected with HCV and many with HIV. Available evidence suggests that during this period not only was the Government actively pursuing the policy of self-sufficiency, but NANBH was perceived as a mild, and often asymptomatic disease, and the advantages of treatment with factor VIII concentrates far outweighed its potential risks. This view was supported by patients, their physicians, and the Haemophilia Society. From the early 1980s, BPL attempted to devise an effective viral inactivation procedure. Progress was hindered by the heat sensitivity of factor VIII and lack of an appropriate animal model to investigate the efficacy of heat-treated products. However, by the time it became apparent that NANBH was more serious than initially thought, all domestic and imported concentrates were already routinely heat-treated and therefore conferred little risk of infection with NANBH or HIV.