CBL/8

NOT FOR PUBLICATION

CBLA ACCOUNTABILITY REVIEW

NOTE OF DHSS/CBLA FOLLOW-UP MEETING OF 15TH OCTOBER 1986

Present

Mr M Harris (Chair))
Dr A Smithies) DHSS
Dr R Moore)

Dr R Lane) CBLA
Mr W Armour)

In Attendance:

Mr M H Arthur DHSS

The Concept of Self-Sufficiency

1. The DHSS related comments to Dr Lane's memo of 19 September 1986. The DHSS were sceptical about the capacity of NBTS to collect 540 tonnes of plasma; an increase in BPL's yield of F8 was sought instead; demand was considered likely to be static; the haemophiliac population was expected to decrease because of genetic counselling; genetic engineered F8 would also become available.

2. In response, CBLA hoped that genetic counselling would be effective, but disputed that there was any decrease in registered haemophiliacs. They considered a return of full confidence in heat-treated Factor VIII (F8) would increase demand beyond the current 80 million ius per annum. CBLA added that recombinant F8 would require scrupulous validation; its uptake for home therapy could not be estimated nor could the total demand of the country's 2,500 haemophiliacs. Based on Scottish proposals, the equivalent target for England and Wales would be circa. 170 million ius; they thought it logical to set the target at around 120 million ius.

3. CBLA said that the benefits of expression of cloned F9 differed substantially from F8; it was not an unstable protein and BPL could presently make a product free from viral activity. If there was a certainty of genetic F8, then the future role of many institutions including BPL would need to be re-examined. CBLA had no licence for downstream exploitation but saw a functional role for 20 years hence.

4. The DHSS accepted BPLs credentials for such work, but said that the aim instead had been to recover investment cost from the production of F8 from human sourced plasma; the fast-track concept had been agreed with this in mind. Dr Smithies asked CBLA to comment on the possibility of obtaining a higher yield.

5. CBLA said that a high grade starting plasma, eg from plasmapheresis, was an advantage. An R & D allocation would assist; they could not forecast future yield, but considered a

doubling of available F8 from human sourced plasma was possible.

6. DHSS said there was little likelihood of RHAs achieving even higher plasma targets. CBLA said that 4 RHAs had shown the way and that 9½ tonnes per million was achievable through the use of SAG(M). Clinicians had shown that they were prepared to accept concentrated red cells and this was an ecomonic form of plasma collection; in addition over 100 plasmaphersis machines were on order and another 100 tonnes could be collected via that route.

7. The DHSS did not accept this as there were a number of RHAs who could not meet even existing targets; a target of 435 tonnes would give albumin too, but an extension to 540 tonnes could only benefit haemophiliacs.

8. CBLA said that the NHS requirement for albumin was not known. If there was an excess market, that product would also produce a return. Use of recombinant F8 would represent a large investment in US industry, whereas money invested at home would carry through the NBTS and would not be lost. Variations of yield meant that plasma targets required revision.

9. The DHSS said they would consider CBLAs comments but there were also ethical considerations such as red cell wastage; an increased use of blood collection was not an answer. One option under consideration at DHSS was a restructuring of plasma procurement targets.

Financial Accountability - Agreed Return

10. CBLA said they had been chastised for spending, or not spending if 31 March intervened. Prices have been one major problem resolved by inclusion in the Memorandum Trading Account. The CBLA would advise DHSS of any remaining concerns.

11. CBLA and DHSS views differed on the meaning of agreed return. The CBLA sought to maximise to achieve a better return on overseas sales. DHSS reported that the objective was an agreed target return on sales and that cash flow problems were secondary to this objective. The Authority should:-

i. get a net return on capital;

ii. forecast cash flow to be compatible with Cash Limit requirements applicable to all SHAs.

The DHSS were looking separately at Mr Smart's proposals.

Genetic Engineering of Therapeutic Blood Products

12. The CBLA explained their view that they needed to expand into genetically engineered products; they quoted specific examples of human sourced reagents which were being replaced by monoclonals. They considered that they could either follow this trend or go out of business; they had no dealings in recombinant F8 but had access to cloned F9. It was noted that the development of monoclonal Anti D was being pursued in a number of Centres. Demand would expand and to continue to provide a plasma sourced supply would be unethical. Albumin, human immunoglobulin and others were obvious candidates for this alternative development; immediately they wished to look at Anti D and cloned F9 to keep Elstree in the forefront of separation technology. They wished to apply this expertise to downstream monoclonals and products from recombinant sources; CBLA regretted that Elstree was not built to deal with expression.

13. In response, the DHSS said that support from the public purse could not be guaranteed when CBLAs present technology became outdated. When human sourced materials were no longer involved no public sector interest would remain. Because CBLA already had some expertise in monoclonals, their development of diagnostics could be endorsed. However at the Accountability Review it had been made clear that development of therapeutic materials should be with a collaborator. Dr Smithies asked about collaboration with others interested in expression, eg Wellcome's collaboration with a firm producing genetically engineered F8.

14. CBLA said that Wellcome had not honoured a commitment between respective Chairman on the joint development of diagnostic tests. CBLA wished instead to move into a range of products in partnership, eg with Celltech and Bioscot, to gain expertise in expression technology.

15. DHSS expressed doubt that CBLA were natural collaborators. CBLA disputed this, they had been asked to manufacture antithrombin 3 for West Germany. They had also worked with Beecham who wanted plasminogen; however many collaborative ventures had been unhappy ones, eg with Speywood.

16. CBLA sustained the view that BPL viability must be maintained by creating a broader technological base with supporting financial arrangement. This would give British Industry an organisation competent to deal with human sourced materials until they were no longer needed. Serious consideration should be given to the commercial $^{2}/_{3}$ rds of BPLs activity.

17. CBLA emphasised that without such involvement BPL would go out of business as a downstream processor once human source material became passé.

18. The DHSS explained that they differed with CBLA over involvement in bioengineering. CBLA said that such technology had stood still in the UK and explained the difficulties. They added that the first person to produce a recombinant F9 would have an excellent market, but this trade would not come to the CBLA unless they were given the go ahead to take forward the fruits of Professor Brownlee's research work.

19. Dr Smithies asked how BPL intended to deal with therapeutic monoclonal Anti D which was regarded as a half-way house.

20. CBLA advised that they hoped to utilise the work being done presently in Bristol and Cambridge; CBLA had the competence to grow the cell lines and hoped to develop in collaboration with Biotest.

21. The DHSS undertook to pursue the possibility of DTI funding for BPL as part of that Department's role in supporting British technology; no further investment could be made at NHS expense.

Manufacture of Diagnostic Kits

22. DHSS expressed the view that the manufacture of diagnostic test kits for outside consumption was not an acceptable CBLA activity.

23. CBLA said that their internal QC was best served when it extended to the NBTS as a plasma supplier. Some plasma batches had been wrongly designated as HIV negative. CBLA had been able to identify hepatitis positives because they possessed their own test. CBLA had a good R1A tests, but foresaw tests being required for HIV, HB, ALT and anti-core. They thought CBLA should develop these in collaboration with British Industry; they could find a large market abroad. A collaboration with Wellcome on an ELISA test had broken down, but they thought they could still make a good HIV test to run with Hepatitis B.

24. DHSS questioned the need for another HIV test kit. CBLA did not believe a Wellcome monopoly should be secured and sought to develop a good recombinant system to challenge this. Dr Lane retained his right to re-test plasma to safeguard his legal position.

25. DHSS agreed to explore how Wellcome could be asked to provide QC assurances on their HIV test perhaps validated by third parties to give CBLA the security they needed. Meanwhile the CBLA work should remain focussed on in-house [illegible] diagnostic kits for QC only.

Research Programme

26. The DHSS had now seen the CBLA research programme, but did not consider it related strategy and objectives.

27. CBLA disputed it was ad-hoc. Research was either product, process or QC related. Six monthly meetings were held on research policy and they maintained DHSS attended their Research Committee. DHSS did not dispute that the Research Committee was attended but this Committee did not discuss research at BPL.

28. The DHSS said that the overall thrust of research must be apparent if bids were to be successful. This was opposed by CBLA; disciplinary strictures could inhibit fortuitous discoveries such as F8Y

29. DHSS insisted that a research framework should be produced to relate objectives of the Authority to timescales.

Pilot Plant

30. The DHSS had received an investment appraisal seeking an additional £8m for a pilot plant. They reminded the CBLA that they have been asked to pursue a 'make do and mend' solution; there was no possibility of a further £8m allocation from public funds.

31. DHSS said that lack of a pilot plant facility need no jeopardise licensing; CBLA disputed this. A large part of the project development could take place in an unlicensed facility but for validation and proper control of viral inactivation they needed premises separate from the main licensed building. PFL Oxford was extended beyond its capabilities and lacked the necessary containment. Building 25 was a possibility but would need a large investment; spiking of the whole pilot plant would be required virus partitioning would not be adequate.

32. The CBLA sought also to meet FDA requirements to protect their overseas markets. DHSS repeated that FDA requirements should not be allowed to inhibit development.

33. DHSS asked about the programme for development of intravenous immunoglobulin. CBLA said that they would invite the CSM to allow use of Scotland's procedure. As a licensed manufacturer BPL could claim it was valid in their hands too. BPL expected in the short-term to be able to meet the demands of the home market.

34. CBLA sought a statement on Crown privilege to clarify their operational position. This was being cleared and DHSS would advise.

35. DHSS asked CBLA to consider how they could meet pilot plant requirements within a budget circa £1m.

Issues Relating to Plasma Supply/Progress Report on NBTS Study

36. It was recorded that this study was underway and a report was due in Summer 1987. The CBLA would also be visited by the study team.

Capital Project

37. A date for the DHSS/Matthew Hall meeting was discussed. A meeting with Minister for Health was anticipated the following week to discuss CBLA Cash Limits.

Strategy for Obtaining Management Information

38. CBLA reported progress; they had appointed a new cost accountant and the stock was being re-valued. They were working to avoid a qualification of their accounts. Discussions with Mr Brownlee would be summarised to the Department by 22 October.

Information for 87/88 Operating Plan

39. DHSS expected supply, demand and price to now be firm estimates, although the general format was approved. The CBLA explained that the Budget proposals for next year were being examined by Deloittes.

Any Other Businees

40. The forthcoming 'stock out' situation of plasma for Anti D immunoglobulin was discussed. It was anticipated the shortage would be for a six month period. CBLA expressed dissatisfaction at RTCs lack of co-operation. Dr Lane proposed to travel to Dublin to try to arrange a short term supply of suitable plasma. He needed to know from DHSS otherwise what finances would be provided for purchase of commercial product probably from Cutters. CBLA envisaged cost would be in the £½ to £1m range.

41. One batch of BPL plasma was being held because a contributor to the pool had developed a sarcoma. It was decided not to pursue a release option and to purchase commercially. The DHSS would lend all possible assistance.