The BSE Inquiry / Statement No 331

Dr TWA Little

(not scheduled to give oral evidence)

THE BSE INQUIRY

STATEMENT OF DR T W A LITTLE

1. This statement is given by Dr Thomas William Anthony Little (TWAL). I am currently Chief Executive of the Veterinary Laboratories Agency (VLA) and my professional address is New Haw, Addlestone, Surrey KT15 3NB.

2. In 1966 I joined the Central Veterinary Laboratory (CVL).3. In the period 1973 - 1996 I held the following posts:

- 1973 - 1982 Senior Research Officer
- 1982 - 1985 Deputy Regional Veterinary Officer (Tolworth)
- 1985 - 1986 Veterinary Head of Section (Tolworth)
- 1986 - 1990 Deputy Director of the CVLThis included responsibility for the Veterinary Medicines Unit and the Biological Products and Standards Department most of which became part of the Veterinary Medicines Directorate in April 1989.
- 1990 - 1996 Director and Chief Executive of the CVL which become the Veterinary Laboratories Agency on merger with the Veterinary Investigation Service in 1995.

4. When I returned to the CVL in 1986 as one of two Deputy Directors I took over specific responsibility for veterinary medicines. This involved fairly frequent contact with the Veterinary Medicines Division and the Animal Health Groups in Tolworth. The Veterinary Medicines Division dealt with the policy and administration side of veterinary medicines. I also briefed the Chairman of the Veterinary Products Committee (VPC) before meetings and attended meetings of the VPC. I chaired the meetings of the Scientific Secretariat of the VPC and the Biologicals Committee of the VPC. I also attended meetings of the Medicines Commission and various other committees which dealt with human medicines when necessary. This included the Committee on Safety of Medicines (CSM) Sub Committee on Biological Products. I also attended occasionally meetings of the Committee of Veterinary Medicinal Products (CVMP) in Brussels.

5. Within CVL I had responsibility for:-

- The Medicines Unit - headed by Alastair Kidd
- The Biologicals Products and Standards Department - headed by Dr Denise Thornton

- The Cattle Breeding Centre in Reading headed by Dr Peter Lamont
- The Animal Production Department headed by Robert Saunders
- The Epidemiology Department headed by John Wilesmith

6. The Medicines Unit statutory function was to provide guidance to the pharmaceutical industry on the preparation and submission of applications for all types of Veterinary Products Licences and Animal Test Certificates issued under the Medicines Act 1968. Applications accompanied by data on safety, quality and efficacy are then assessed by veterinary, pharmacy and scientific staff in preparation for consideration by the independent Veterinary Products Committee.Several EC Directives also impinged on the statutory work carried out bythe Medicines Unit, in particular, directives dealing with the standards and procedures required for marketing veterinary pharmaceutical medicines, the directive concerned with feed additives and the directive concerned with humans.*(MAFF - Research and Services - Central Veterinary Laboratories and the Veterinary Investigation Centres 1986)* (Annex 1) **(YB 86/00.00/1.1-1.8)**

7. The Biological Products and Standards Department statutory functionsincluded:"Examination of, and advice on, applications submitted under the Medicines Act and the Therapeutical Substances Order for licences to market veterinary immunological products (in conjunction with the Medicines Unit). Testing of samples of such products for safety, efficacy and quality, the scrutiny of manufacturers' test protocols and the development and evaluation of test methods. Providing British Standards for use in quality control tests. Inspection of the manufacture of veterinary immunological products.*(MAFF - Research and Services - Central Veterinary Laboratories and Veterinary Investigation Centres 1986)* (Annex 1) **(YB 86/00.00/1.1-1.8)**

8**. Chronology in relation to Veterinary Medicines 1986 to March 1989**November 1986 BSE first recognisedEarly 1987 TWAL aware of the existence of BSE through contacts

with Dr Watson, the Director of CVL and Dr Shreeve, the Deputy Director who took the lead on BSE and research matters

May 1987 John Wilesmith formally involved and starts epidemiological investigations.

29 May 1987 Gerald Wells presents paper to the Veterinary MedicalResearch Club.

15 June 1987 John Wilesmith involves Alastair Kidd (Head of Medicines Unit) in consideration of possible involvement of Organophosphates and synthetic pyrethroids.

7/8 July 1987

Progressively during 1987 staff at CVL become aware of and discuss

informally the potential of BSE to contaminate immunological products. Such

concerns were discussed with administrators in the Veterinary Medicines

Division. Following Wells et al publication TWAL discussed with Prof J

Armour, Chairman VPC.

November 1987 As a result of informal discussions, Peter Luff was asked to produce a paper on BSE - implications for biologicals products.

6 January 1988 Biologicals Committee of VPC. Peter Luff's paper

tabled (Annex 2)**(YB 88/01.06/1.1-1.5)** detailed discussion at next meeting.

3 February 1988 Biologicals Committee of VPC (chaired by A Kidd)

(Veterinary Medicines Division represented by Mr Muriel and Mrs Buckler)

Detailed discussion of Mr Luff's paper. **(YB 87/12.00/1.1-1.3)** Report to senior officers in MAFF (CVL, VMD and AH Division) further consideration of whether certification of cattle for freedom from BSE was possible. (Annex 3) **(YB 88/02.03/1.1-1.2)**

During the next few months, discussions were held with staff of the National Institute for Biological Standards and Controls (NIBSC) leading to arrangements for a meeting at NIBSC by Dr P Minor.

16 May 1988 Meeting at NIBSC attended by Mr J Wilesmith CVL,

Drs R Ridley and H Baker MRC, Dr Schild, Minor and Ferguson NIBSC and Drs Beale and Garland Wellcome Laboratories.Recommendation of this meeting (Annex 4)**(YB 88/08.00/2.1 ; YB 88/07.11/13.1 ; YB 88/05.16/2.1-2.12)** sent to Julymeeting of Biological Sub committee of CSM.

7 June 1988 Biologicals Committee of VPC

Agreed to a set of guidelines for pharmaceutical industry produced by Geoff Wood.

Further internal meeting to be arranged between CVL staff to progress the guidelines and any urgent matters relating to products. (Annex 5) **(YB 88/06.07/10.1-10.6)**

8 June 1988 Internal CVL meeting to discuss the implications of BSE to Biologicals Products containing bovine extracted material (Annex 6). **(YB 88/06.08/11.1-11.2)** Following a detailed review of situation the following recommendations were made:1.

Specific concern over use of pituitary gland

products by veterinary surgeons and companies. Paper to be produced for Tolworth (Veterinary Medicines Division).

2. Urgent review of all products both immunological and pharmaceutical for possible inclusion of ingredients of bovine origin.

3. Draft guidelines to be presented in full to the National Office of Animal Health (NOAH), the trade body representing the Veterinary Medicines part of the pharmaceutical industry, at next meeting on 11 July 1988

5 July 1988 Biologicals Committee Meeting

Detailed discussion of Geoff Wood's draft guidelines (SP3875.2) (Annex 7) **(YB 88/07.05/6.1-6.4)**Major concern over pituitary gland products and a letter being sent to all licence holders. Amended paper to be presented to NOAH on 11 July and sent to NIBSC and DHSS.

11 July 1988 Meeting with NOAH. (Annex 8) **(YB 88/07.11/12.1-12.4)**Dr Little briefed the meeting on the emergence of BSE and showed the MAFF Video.Mr Wood presented the proposed guidelines which were discussed. Mr Cook on behalf of NOAH agreed to comment as soon as possible and agreed to obtain information on pharmaceutical products which contained bovine material of UK origin.

6 September 1988 Biologicals Committee of VPCSome replies from companies using pituitary glands in their products received. Copies of draft guidelines have been sent to NIBSC and DHSS. (Annex 9) **(YB 88/09.06/5.1-5.4)**

8 November 1988 Meeting with NOAH. (Annex 10)**(YB 88/11.25/5.1 ; YB 88/11.08/5.1-5.6)**

Dr Little briefed the meeting on the current BSE situation. Some problems with implementing the guidelines were discussed but NOAH were keen to see them published quickly.

20 December 1988 Letter from Sir Richard Southwood asking what

detailed consideration had been given to this issue and asking for views on whether some form of guidance to industry might be useful. (Annex 11) **(YB 88/12.20/2.1)**

3 January 1989 Meeting between Medicines Division of DHSS (Dr Adams, Dr Jeffreys and Dr Purves) and MAFF (CVL) (Dr Little, Mr Kidd and Mr Bradley) Detailed review of the

situation and the need to 'keep in step'. A further meeting to be held after MAFF guidelines have been reviewed by the VPC at its January meeting. (Annex 12) **(YB 89/01.03/2.1-2.2)**

19 January 1989 Veterinary Products Committee

The draft guidelines to assist manufacturers of biological products containing materials of bovine origin was provided for members' comments. Mr Ray Bradley provided members with an extensive briefing on the BSE problem. Written comments on the guidelines were requested before the February meeting. (Annex 13) **(YB 89/01.19/6.1 ; YB 89/01.00/2.1-2.3)**

26 January 1989 Reply sent to Sir Richard Southwood (Annex 14) **(YB 89/01.26/2.1-2.4)**

1 February 1989 Meeting between MAFF officials (Dr Little, Mr Kidd, Mr Bradley) and D of H (Drs Jeffrey and Adams) from Medicines Division) plus representation from NIBSC and Biologicals Committee of CSM.The meeting agreed the text of what were now joint MAFF/DH guidance for manufacturers plus a timetable for clearance by various advisory committees to enable publication in MAIL before Easter.

15/16 February 1989 Veterinary Products Committee Meeting (Annex 15)

(YB 89/02.15/6.1 ; YB 88/02.15/7.1)VPC (89) 38 containing the revised CSM/VPC guidelines for industry were presented for comment together with the correspondence with Sir Richard Southwood.Subject to some minor changes the Guidelines were agreed.

22 February 1989 Human and Veterinary Medicines Briefing Group on BSEThe meeting was called to consider the DH/MAFF draft guidelines to advise CSM. The meeting consisted of members of the Biologicals Sub Committee of CSM, invited experts, representatives of the Department of Health Medicines Division, the Department of Health and MAFF prior to the publication of the Southwood Report (Annex 16) **(YB 89/2.22/11.1-11.8)**

7 March 1989 Biologicals Committee of VPCA joint set of guidelines had been agreed with D of H. A separate (MAFF) questionnaire had been prepared asking for details of all products had been sent out to all licence holders for reply by May 1989. (Annex 17)**(YB 89/03.07/2.1-2.5)**

21 March 1989 Meeting with NOAH (Annex 18) **(YB 89/03.21/13.1-13.4)**Dr Little outlined the current situation and explained why members had received the guidelines from both D of H and MAFF. He explained that the guidelines set a very high standard but indicated that manufacturers may present equivalent methods to obtain the required standard.

1 April 1989 VMD establishedColleagues from Veterinary Medicines Division, the Medicines Unit and part of BP&S join up to become the VMD as recommended by the Cunliffe Review. Dr Rutter was appointed as Chief Executive designate. I moved on to take over the Agency Project Team for CVL.

Contact with the Department of Health

9. I have been asked specifically about my attendance at the Biological Sub Committee of the CSM. (Annex 19) **(YB 87/09.09/1.1-12)**

10. On 9 September 1987 I attended a meeting of the Biological Sub-Committee of the CSM. This Sub-Committee is made up of independent experts. The function of the Sub-Committee is to advise the Committee on Safety of Medicines, which is also made up of independent experts. A number of officials, mainly from the Department of Health, attend both committees. Both committees advise on the safety of human medicines, including vaccines, but do not normally address matters relating to animal health.

11. The 9 September 1987 was (I believe) the only time I attended a meeting of the Biological Sub-Committee. On this occasion, I attended in place of the usual MAFF representative, Dr Brinley-Morgan who retired in 1986.

12. A copy of the minutes of the meeting is Annexed to this statement. **(YB 87/09.09/1.1-1.12)** The meeting was chaired by Professor Collee, who had lectured to me in Edinburgh when I was an undergraduate. Dr Paul Adams was also at the meeting. I knew him as we both attended as officials the Veterinary Products Committee meetings and were both members of that Committee's Scientific Secretariat. I do not believe I knew any of the other attendees at the meeting personally.

13. One of the products discussed during the meeting was composed of human dura mater. This was under review at the meeting because of a case of CJD associated with its use. The official from the Department of Health presenting the case was Dr Adams.

14. Although the minutes of the meeting make no reference to it, I made a mention at the meeting of the occurrence of BSE in cattle. I believe (although I cannot now be sure) that I mentioned BSE during the course of the formal meeting. I can remember that a discussion of scrapie resulted from my mention of BSE. Professor Collee impressed me with his knowledge of scrapie. It may be that my mention of BSE and Professor Collee's comments on scrapie arose during discussion on Dr Adams's paper on the dura mater products.

15. Although I am uncertain about the precise context in which I raised BSE, I am certain that Professor Collee and Dr Adams were present when I mentioned BSE.

16. I also believe that Dr Adams introduced me to a number of his colleagues from the Department of Health after the meeting, although I cannot remember who they were. We most probably informally discussed BSE in relation to the use of bovine material in medicinal products, both human and veterinary.

17. I am not aware of any action taken by the Department of Health or the Biologicals Sub-Committee as a result of my mention of BSE at this meeting. I have seen a minute from Dr Watson to Mr Rees of 10 September 1987 **(YB 87/9.10/1.1)**

18. I believe the minute accurately reflects what I told Dr Watson. It was my

understanding that someone from the Department of Health would be writing or otherwise getting in touch with MAFF.

19. There was frequent contact between myself and other senior CYL staff with the D of H Medical Assessors who attended the VPC meetings and the Scientific Secretariat. Normally either Dr Paul Adams, Dr Geoffrey Diggle or Dr Kevin Woodward attended.

20. There was a good working relationship. As can be seen from the chronology there was also contacts with NIBSC which performed a role for D of H which was similar to that which CVL carried out for MAFF.

21. At this stage it is difficult to determine when BSE was first discussed in these informal discussions. Formal meetings are listed in the chronology.

Southwood Committee Recommendation - 24 February 1989

22. One of the Southwood recommendations (8.2) was "the attention of the Licensing Authority, the CSM and the VPC be drawn to the emergence of BSE so that they can take appropriate action".

23. From the chronology it can be seen that the Biologicals Committee of the VPC were alert to this problem from November 1987 and had commissioned papers and the draft guidelines which were made available to the Southwood Committee.

24. The full VPC considered the guidelines in January 1989.

Contacts with the Pharmaceutical Industry

25. As can be seen from the chronology, the draft guidelines were first given to NOAH in July 1988 for their comments and contact was being made with product licence holders in June 1988 regarding some specific products.

26. The industry started searching for alternatives to UK bovine products at an early stage and were anxious to protect the safety aspect of their products.

27. Meetings with NOAH also took place in November 1988 and March1989.

28. The Consultative Committee chaired by Dr Tyrrell recommended in its Interim Report (June 1989) that there should be more detailed investigations into the fate of bovine and ovine tissues which might lead to the spreading of infection.

29. Urgent activity on the veterinary aspects of inclusion of bovine material in vaccines and other drugs (mainly hormones) commenced in June 1988 and a detailed questionnaire was circulated in May 1989.

30. There was similar activity by the medical assessors of the CSM.

31. Dr Tyrell was a member of the Biologicals Sub Committee of the CSM at this time.

Diagnosis of Scrapie and BSE by the Veterinary Investigation Service

32. I have been asked to comment on this matter. Between 1982 and 1985 I was a Deputy Regional Veterinary Officer based at Tolworth in the Veterinary Investigation Section which managed the VI Service. I was a frequent visitor to VI Centres and was particularly concerned with project work. In 1995, the VI Service merged with the CVL

to form the VLA of which I am currently Chief Executive and Director.

33. At the time of the first cases of BSE (in the mid 1980s) there were many veterinarians in the VIS with experience in general histopathology. This experience was promoted and encouraged through regional, informal meetings of the Histopathology Study Groups, at which participants from Veterinary Investigation Centres ("VIC"), the CVL and Veterinary School Pathology Departments would discuss cases.

34. Although not every Veterinary Investigation Officer ("VIO") was trained in histopathological diagnosis, and not every VIC had the capacity to process tissue samples for histopathology as a routine, all VIOs considering a clinical differential diagnosis of neurological disease would have collected material for histopathological examination and referred it to a colleague with the necessary expertise. The colleague could have been within the VICs or the in the Pathology Department at CVL or at the Lasswade Laboratory. Some of these VIOs with an interest and experience in histopathology would also have had formal training in pathology, but very few would, at that time, have claimed complete confidence in making histopathological examinations of brain or other nervous system tissues.

35. If the indication, particularly from the case history, was that an unusual neurological problem was occurring, the VIO usually referred the whole fixed brain, intact, direct to the Consultant Pathology Unit ("CPU") at CVL. The exception to this would have been the examination, by VIOs in some instances, of brains of sheep for diagnosis of scrapie and ruminants generally, for diagnosis for listeriosis. However, brain material from some scrapie cases was passed to the CPU, CVL sometimes for primary diagnosis or for second opinions.

36. Very few cases of neurological disease in adult cattle were presented to VIOs for post mortem examination and thus the examination of cow brains by any pathologist at that time was a relatively rare event.

37. The original cases to be diagnosed, of the disease which later became known as BSE, were referred to by Mr Carl Johnson a VIO at Wye VIC, Kent, to Mr Gerald Wells at CVL but, as Dr Matthews statement indicates, another case was diagnosed at a VIC. The transcript of Dr Matthews statement states: "Roger Hancock, who I think first picked [it] up down in the south west."

38. Roger Hancock was a VIO working at the Truro VIC who had experience of the histopathological diagnosis of scrapie. He was thus able to recognise similarities between spongiform changes in scrapie and those found in a brain of a cow submitted to him. In view of this highly unusual finding, tissues from the case were submitted to Mr Wells at CVL for a second opinion.T W A Little

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OTHER DOCUMENTS ANNEXED TO DR LITTLE'S STATEMENT CAN BE FOUND AT THE FOLLOWING YEAR BOOK REFERENCES

YB 89/1.9/3.1-3.3

YB 90/11.00/5.1-5.2 attaching YB 89/03.15/4.1-4.4

YB 88/11.02/5.1

YB 88/12.07/1.1

YB 88/11.14/2.1