'89 02-14 14:56 01

APPENDIX 2

TELEFAX TO DR. PAUL ADAMS - ROOM NO. 1526

FROM DR.

TELEFAX NOS.

No. of pages: 5 including this cover page.

Date of transmission: 14th February 1989

CONFIDENTIAL

Answers provided to Dr. Paul Adams of the CSM on 14th February 1989.

1. Medical Vaccines and therapeutic proteins, licensed or in clinical trial: which products contain material of bovine origin?

2. Which is the country of origin?

PRODUCT:	PRESENCE OF BOVINE MATERIAL
ORAL POLIO VACCINE	Foetal calf serum, New Zealand origin since mid-1988. Earlier foetal calf serum, UK and NZ origin. Commercial supply from third parties. Used only in cell growth stage.
ALMEVAX RUBELLA	No bulk made since 1978, used Foetal calf serum of UK and NZ origin of commercial supply from third parties for cell growth stage.
ARILVAX YELLOW	No bovine material incorporated.
DIGIBIND	No bovine material incorporated.
WELLFERON	Adult bovine serum, UK origin for cell growth. Purified through process that substantially removes bovine serum. Process destroys or eliminates scrapie agent. Once existing serum stocks are exhausted the process will utilise serum from areas free of BSE. Immunoaffinity sera of UK origin used in downstream processing. Produced in house. Diet free of BSE risk fed to donor cattle since mid-1988.

PRODUCT:	PRESENCE OF BOVINE MATERIAL
	Adult bovine serum. UK origin, for cell growth. Purified through a process which substantially removes bovine serum. Will utilize only New Zealnd sourced adult bovine serum from March 1989. Immunoaffinity sera of UK origin used in downstream processing. Produced in house. Donor animals fed only BSE risk free diet since mid-1988.
DIPHTHERIA	Oxheart: beef muscle digest produced in house. Of UK origin to mid-1988, Southern Irish origin subsequently. Now seeking sources free of BSE.
TETANUS	Calcium Casein and acid hydrolysed casein digest of UK (Scotland) origin from Bullocks heart infusion broth produced in house. UK origin. Bullocks heart of Southern Irish origin from mid-1988. Now seeking sources free of BSE.
DIPHTHERIA AND TETANUS	As above.
PERTUSSIS	Acid hydrolysed Casein digest of UK (Scotland) origin from Single large bulk supply lasts for many years.
TRIVAX DIPHTHERIA,TETANUS PERTUSSIS	As above
CHOLERA) TYPHOID)	Horse muscle digest. UK origin.

PRODUCT:	PRESENCE OF BOVINE MATERIAL
	Horse muscle digest and Ox liver digest, origin. Used only in Papua, New Guinea.
	Casein digest as above. Last bulk prepared 1978.
	No bovine material incorporated.

3. How much bulk stock of product has been manufactured since 1980?

4. What are the current stock levels?

PRODUCT	UNIT	BULK MADE SINCE 1980 (Approx)	CURRENT STOCKS* (Approx)
	DOSES	6.6 million	1.1 million
	DOSES	8.5 million	0.7 million
	DOSES	47.6 million	1,300L bulk and 4.25 million doses.
	LITRES	5,573	460
	LITRES	11,435	820
	LITRES	643	10
	LITRES	23,215	1,250
	LITRES	14,930	750
	LITRES	5,009	488
	DOSES	Made prior to 1980	33,832 doses.
	LITRES/MU	3.0 million L	1.7 mega units.
	VIALS	29,000	7,400

*Stocks shown are in the final stages of manufacture at Additionally there are stocks in earlier stages of process and material in the distribution chain. Material in the earlier stages cannot be simply expressed as final doses.

5. How long would it take to switch to non UK bovine origin material?

To change all bovine material sources from UK to non UK source will take approximately 18 months but stock will last a variable time.

6. How long would it take to switch to non bovine material?

To change to non bovine material will take at least five years and would involve clinical equivalence testing.

Dr.

Telephone:

Fax:

Appendix 3

HUMAN & VETERINARY MEDICINES WORKING GROUP RE BSE

MEETING 22/2/88 AT 10.00AM AT MARKET TOWERS

Members invited to attend: Chairman Professor Collee

Biologicals Subcommittee

Professor Collee
Dr Schild
Dr Minor
Dr Tyrell

Invited Experts

Dr Klinberlin
Dr Martin

MAFF

Dr Little
Mr Kidd
Mr Bradley
Mr Wilesmith
Mr Scolan

Medicines Division

Dr Adams
Dr Jefferys
Dr Rotblat
Dr Purves
Mr Sloggem
Mr Bewley
Mr Love
Mrs Alderman
Mr Askins

Other DH

Dr Pickles
Mr Cunningham
Dr Salisbury
Mr Colman
Dr Sutton

For Information

Dr Jones
Mr Wilson

14/02/89 14:47 002

APPENDIX 4

VETERINARY PRODUCTS COMMITTEE

Chairman		
*Professor J Armour PhD Dr(hc) (Utrecht) MRCVS	Dean of Faculty of Veterinary Medicine and Titular Professor in Veterinary Parasitology University of Glasgow	
Members		
*Professor P M Biggs CBE DSc DVM(hc) PhD BSc FRCVS FRCPath CBiol FIBiol FRS	Director of Animal Disease Research, Agricultural & Food Research Council	Houghton Poultry Research Station, Houghton Huntingdon PE17 2PA
°Professor PG Blain BMed Sci MB BS MRCP CBiol MIBiol	Professor of Occupational Health & Hygiene, University of Newcastle Upon Tyne	Dept of Occupational Health & Hygiene University of Newcastle Upon Tyne NE2 4HH
*Professor J W Bridges PhD BSc CChem MRC Path FRSC FIBiol MIEnvSci	Professor of Toxicology and Director of the Robens Institute University of Surrey	Department of Environmental Health Robens Institute University of Surrey Guildford, Surrey
*Professor J R Brown PhD MSc BSc FRSC CBiol MIBiol MPS CChem	Head of Department of Pharmaceutical Chemisty Sunderland Polytechnic	Department of Pharmaceutical Chemistry Langham Tower Ryhope Road Sunderland SR2 7EE
*Mr D S Collins MVB MRCVS	City Veterinarian Belfast	
+Mr P J Crossman MSc BVetMed MRCVS	Practising Veterinary Surgeon Chichester West Sussex	
*Dr P E Jacobs PhD BVMS MRCVS	Reader in Veterinary Parasitology Royal Veterinary College	The Royal Veterinary College University of London Hawkshead House Hawkshead Lane North Mimms Hatfield Hertfordshire AL9 4TA

*Professor J O Jarrett PhD BVMS MRCVS	Titular Professor of Veterinary Pathology University of Glasgow	University of Glasgow Veterinary School Bearsden Glasgow G61 1QH
*Professor R W Lacey MD PhD MB BChir BA DCH MRCPath	Professor of Clinical Microbiology University of Leeds	Department of Microbiology University of Leeds Leeds West Yorkshire LS2 9JT
+Professor G E Lamming OBE DSc PhD MS BSc(Agric) FIBiol NDA	Department of Physiology & Environmental Science University of Nottingham	Department of Physiology & Environmental Science School of Agricutlure Sutton Bonington Loughborough Leics LE12 5RD
*Dr P Lees PhD BPharm	Department of Physiology & Chemistry Royal Veterinary College University of London	Department of Physiology Royal Veterinary College Royal College Street London NW1 0TU
°Dr F de Matteius PhD	Toxicology Unit Medical Research Council	Medical Research Council Toxicology Unit MRC Laboratories Woodmansterne Road Carshalton Surrey SM5 4EF
*Professor I M Smith PhD MSc MRCVS	Department of Microbiology & Parasitology Royal Veterinary College University of London	Department of Microbiology & Parasitology Royal Veterinary College London NW1 0TU

Occasional Members

+Professor A H Linton DSc PhD MSc FRCPath	Professor of Bacteriology School of Veterinary Science University of Bristol	Department of Microbiology Medical School University Walk Bristol BS8 1TD
Dr G J Rowlands PhD	Head of Statistics Institute for Research into Animal Diseases	Institute for Research on Animal Diseases Compton Near Newbury

AH/8971L/4

APPENDIX 5

MEMBERSHIP OF THE COMMITTEE ON SAFETY OF MEDICINES 1988

Professor A W Asscher BSc MD FRCP (Chairman)
Dean of St George's Hospital Medical School, London

Professor S S Bleehen B A MB BChir FRCP
Professor of Dermatology, Sheffield University and Consultant Dermatologist Royal Hallamshire Hospital
(Appointed 30 August 1988)

Professor T G Booth OBE BPharm PhD FPS MCPP
Professor of Pharmacy Practice, University of Bradford

Professor A M Breckenridge MSc MD FRCP
Professor of Clinical Pharmacology, Liverpool Unversity

Professor J G Collee MD FRCP FRCPath
Professor of Bacteriology, University of Edinburgh Medical School

Professor P H Elworthy BPharm DSc PhD CChem MRSC FPS MCPP
Emeritus Professor of Pharmacy, University of Manchester
Visiting Professor of Pharmaceutics, King's College and the School of Pharmacy, University of London

Professor A T Florence DSc PhD FRSC FRSE FPS
Professor of Pharmacy, University of Strathclyde
(from 1 January 1989, Dean of the School of Pharmacy, University of London)

Professor M W Greaves MD PhD FRCP
Professor of Clinical Dermatology, St John's Hospital for Diseases of the Skin, London
(resigned 31 July 1988)

Professor H S Jacobs BA MD FRCP
Professor of Endocrinology, The University College and Middlesex Hospital School of Medicine, London

Dr W A Jerrett MB BCh FRCGP
General Practitioner, Glamorgan

Professor M J S Langman BSc MD FRCP
Professor of Medicine, University of Birmingham

Professor D H Lawson MD FRCP (Edin) FRCP (Glas)
Consultant Physician in Clinical Pharmacology, Royal Infirmary, Glasgow
Visiting Professor, University of Strathclyde, Glasgow

Mr F E Loeffler FRCS FRCOG
Consultant Obsetetrician and Gynaecologist
St Mary's and Queen Charlotte's Hospitals, London

Professor J O'D McGee MD PhD FRCPath MA (Oxon)
Professor and Head, Nuffield Department of Pathology and Bacteriology
University of Oxford, John Radcliffe Hospital

AH/8971L/5

Professor A E M McLean BM PhD FRCPath
Professor of Toxicology, University College and Middlesex School of Medicine, London

Dr Elizabeth Mayne MD FRCP(G) FRCPath
Consultant Haematologist, Royal Victoria Hospital, Belfast

Professor S R Meadow MA DCh FRCP
Professor of Paediatrics and Child Health
St James' University Hospital, Leeds

Dr S A Montgomery BSc MD FRCPsych DPM Eng
Reader in Psychiatry, St Mary's Hospital, London

Professor G Nuki MB BS FRCP(Ed) FRCP(London) MRCS LRCP
Professor of Rheumatology, Northern General Hospital, Edinburgh

Dr B L Pentecost MD FRCP
Consultant Physician, Birmingham

Professor M D Rawlins BSc MD FRCP (London) FRCP (Edin)
Professor of Clinical Pharmacology, Wolfson Institute of Clinical Pharmacology
University of Newcastle-upon-Tyne

Professor M P Vessey MA MD FRCP FRCPE FRCGP
Professor of Social and Community Medicine, Radcliffe Infirmary, Oxford

14/02/89 09:51 001

Ministry of Agriculture Fisheries and Food

720 5647

APPENDIX 6

FACSIMILE TRANSMISSION FORM

For completion by the originator:

Date 14.2.89 Time 945 No. of pages 145

Name Dave Garrick Extension 4021

Room No. 1003 Building TOKT Division AMD Branch B

Urgency VERY URGENT

Please use BLOCK LETTERS

To:
Facsimile No. (if known)

Full name
and address

From:

Please repeat to:
(a) Facsimile No. (if known)

Full name
and address DR P ADAMS
OH, MARKET TOWERS,
1 NINE ELMS LANE
SW8 5AR, LNE

(b) DR H PICKLES
OH, MARKET TOWERS
1 NINE ELMS LANE
SW8 5AR, LNE

(c) R1525

(d)

(e)

(f)

For completion by operator

Job completed: Date Time Job No. 413

89/02.14/11.11

14/02/89 09:51 002

BSE

Our Minister meets Professor Southwood later today. Due to lack of time it was not possible to clear with you the attached briefing which has gone to him, as per the Vet. medicines contribution to a wider brief. If you have any essential comments, can I have them by 3.00 pm latest today

A J C Taylor
Tolworth Tower Ext 32.

Dr P. Adams
Dr H. Pickles } DH Tolworth Towers

DRAFT

CONTRIBUTION TO COMMENTARY ON SOUTHWOOD REPORT

Veterinary medicines

The Report

1. At paragraphs 5.3.3 - 5.3.5 , the Report assesses the risk that vaccines and other medicinal products derived from animal material. Although the Report recognises that the risk of transmission of BSE to humans is remote, the identification of a substantial range of medicines which could theoretically pose a risk is, in our view, and that of the Department of Health, alarmist. The risk, at least to humans, appears remote and with care it can be minimised.

2. The Report recommends (paragraph 8.2) that the attention of the licensing authority and Veterinary Products Committee be drawn to the emergence of BSE, so that appropriate action may be taken. Such action should cover existing and new products.

Action in hand

3. The VPC has already been consulted about the risks arising from BSE. Draft guidelines to be issued to all manufacturers of medicinal products have been prepared in close consultation with Department of Health staff. These are being considered by the VPC and, in parallel, by the Committees advising on human medicines. A copy is attached.

4. The Minister should note, however, that the guidelines represent a counsel of perfection:

(i) Guidance 1, on the use of defined, BSE-free sources, will be severely restrictive. A number of farms in the UK will meet these criteria but they have not been identified; farms overseas ostensibly meet the criteria but we cannot be sure that non-detection of BSE in all cases equates with

freedom from the disease. Moreover, many countries are unsuitable sources of medicinal material because of other, endemic diseases. New Zealand, ~~and possibly Australia~~ appears the safest source, but their supply is unlikely to match demand.

(ii) Most pharmaceutical companies buy from specialist producers of primary and intermediate material, whose activities lie outside the powers of the Medicines Act. Product licence holders, who are responsible for the quality of their products, would therefore need to secure assurances from their suppliers that the guidance is being respected. This might pose problems in a minority of cases and if serious doubts were to raise about the quality of any product we could withdraw its licence.

(iii) Guideline 4, on collection techniques, conflicts with normal practice in abattoirs, where most material is obtained. This is unlikely to matter if reliable BSE-free sources are used, although a risk of cross-contamination might remain.

(iv) The sterilisation treatment recommended in Guideline 5 is generally inappropriate to biological medicines - which it would destroy - but would be suitable for some tools and equipment.

5. Although NOAH (the National Office of Animal Health, representing animal pharmaceutical companies) accept the need for guidelines, they have not seen the draft, which they may find more rigorous than expected. They may respond by pressing for assistance in complying with the guidelines (eg. by introducing a BSE-free farm certification scheme, extension of Medicines Act controls to primary source suppliers). Any proposals would need to be considered in relation to their likely effectiveness in improving the supply of BSE-free material.

Further action

6. In addition to the guidelines and again in close consultation with the Department of Health, we are drawing up a list of all medicines manufactured from bovine material. This is necessary in order to cover existing as well as new medicines, a point noted in the Southwood Report recommendation. Although some information is readily available, this is not exhaustive, and we shall be writing to each product licence holder requiring them (under the Medicines Act) to provide information in respect of each licensed product on bovine material noted in its manufacture.

7. When the product information has been reviewed it will be possible to determine what, if anything, further should be done to safeguard human and animal health, taking into account the importance of maintaining adequate supplies of vaccines against major human health hazards such as measles and polio.

PROPOSED JOINT CSM/VPC GUIDELINES FOR INDUSTRY

The following guidelines are addressed to product licence holders and applicants.

1. Scope
It is intended that all products licensed under the Medicines Act 1968 for human or veterinary use, that are administered parenterally or to open wounds, should conform to these guidelines if they contain material from a bovine source, or if bovine material has been used during their manufacture.

Although these guidelines relate to BSE and materials of bovine origin, they should also be considered as applicable to material from sheep, goats, deer, and some other animals susceptible to scrapie-like agents, which are not suitable alternative sources.

2. Cattle source
Bovine material should come from cattle, taken from a closed herd in the female line since 1980, in which no animal has been clinically suspected of having BSE, and which has not been fed rations containing ruminant derived protein during that period.

3. Tissues excluded
No nerve or neural tissue, spleen, thymus and other lymphoid tissue, placental tissue or cell cultures of bovine origin should be used in the manufacture of medicinal products.

4. Collection techniques
All possible measures should be taken to avoid contamination of the bovine material with BSE agent, in particular:

no tissue is to be used in medicinal products when collected postmortem from a bovine animal after brain penetrative stunning.

all tissue collected from the bovine animal should be taken aseptically using sterile equipment. Needles, syringes, scalpel blades etc should be disposable items.

it is recommended that whenever possible, source animals should be calves up to 6 months old.

for serum: all cellular components must be removed.

for foetal calf serum: great care should be taken to avoid contamination by placenta and foetal fluids. All cellular components must be removed.

5. Sterilisation
When sterilization procedures are used, they should be demonstrated to be capable of inactivating scrapie-like agents - at present thought to be autoclaving using a porous load cycle at 134°C-138°C for 18 minutes at 30 psi.

6. Product
Whenever possible, the product should be terminally sterilised by a validated method.