

Appendices

	Page
1. Panel membership and acknowledgements	15
2. Background to BSEP	16
3. Grants funded under BSEP Phases 3 and 4	19
4. Questionnaire results and analysis	21

APPENDIX 1.

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APPENDIX 2.

BACKGROUND TO THE BIOLOGY OF THE SPONGIFORM ENCEPHALOPATHIES PROGRAMME

BBSRC (formerly the Agricultural and Food Research Council, AFRC) has supported research into the Transmissible Spongiform Encephalopathies (TSEs) since the early 1990s, through successive phases of the Biology of the Spongiform Encephalopathies Programme (BSEP) and as part of the core programme of the Institute for Animal Health (IAH).

The programme was initiated in response to growing public concern about the outbreak of bovine spongiform encephalopathy in the UK, and was designed to:

- build on existing strengths developed at the AFRC/Medical Research Council Neuropathogenesis Unit (NPU) in Edinburgh; and
- complement and underpin related studies of the transmission and epidemiology of BSE initiated concurrently by the Ministry of Agriculture, Fisheries and Food (MAFF), together with research on Creutzfeldt-Jakob disease funded by MRC and the Health Departments. (In 2001 MAFF was replaced by the Department for Environment, Food and Rural Affairs (Defra).)

BSEP Phase 1

In 1990, AFRC launched Phase 1 of the programme. 22 grants were awarded to a total value of £6.4M, with a further £0.5M being spent on additional core funded research at the NPU and at IAH's Compton Laboratory.

The objectives of Phase 1 were:

- to identify and characterise the infectious agents of BSE and related TSEs
- to investigate the genetic control of host animal susceptibility to TSEs
- to understand the mechanisms of pathogenesis of the TSE agents including those which affect humans

BSEP Phase 2

BSEP Phase 2 ran between 1995 and 1999, and funded 15 grants to a total value of £4.2M.

The objectives of this phase were:

- to identify and characterise the infectious agents of BSE and related TSEs
- elucidation of the molecular basis of strain variation in scrapie
- further development of transgenic animal models for the investigation of the nature of the infectious agent, transmission and species barrier
- to understand the molecular basis of pathogenesis of the TSE agents including those which affect humans
- to investigate the genetic control of host animal susceptibility to TSEs

BSEP Phase 3

A directed programme of research into TSEs involving the Department of Health (DH), MRC, BBSRC and MAFF was set up by the Department of Health in 1996 and led to a joint MRC/DH call for proposals. As it was clear that some of the applications received were appropriate to BBSRC's remit, BBSRC and MRC agreed that BBSRC should take the lead on those proposals, which were managed as BSEP phase 3.

The priority themes for this call related specifically to BBSRC's remit were:

- molecular, genetic, cellular and functional approaches to elucidating mechanisms of TSEs transmission, PrP replication, pathogenesis and clinical progression
- the biological function of normal PrP
- the molecular structure of the prion proteins
- rational approaches to developing therapy

Fourteen grants totalling £6M were made under this phase.

None of the Phase 3 awards were specifically focused on scrapie. However, the value of studies on scrapie as a model TSE in a host animal was identified by the Spongiform Encephalopathy Advisory Committee (SEAC) who recommended that additional research should be funded on the pathogenesis and epidemiology of scrapie. BBSRC invited IAH to submit proposals for a major programme of work including the setting up of a reagent resource centre to service the BSEP as a whole. The proposals were assessed by the BSEP Working Party and external referees, and taking account of views from MAFF, DH and MRC.

Subsequently BBSRC announced awards to IAH for studies on the pathogenesis of scrapie and the epidemiology of sheep, and to establish a resource centre at IAH to supply reagents for research on TSEs to the wider community.

BSEP Phase 4

In March 1998, BBSRC announced BSEP phase 4, which aimed to build on BBSRC's earlier investment and, in particular, encouraged applications that involved collaboration between centres with well-established expertise in TSE research, or between such centres and other groups with complementary expertise. As with the earlier phases, BBSRC also encouraged applicants to ensure their proposals were set in the context of ongoing research supported by the Council and other public sponsors of TSE research. The announcement reflected BBSRC's priorities at that time for TSE research: the molecular structure of prion proteins; the biological function of normal PrP; PrP conversion; pathogenesis and rational approaches to intervention; and molecular, genetic, cellular and functional approaches to elucidating mechanisms of TSE transmission. Sixteen grants were awarded in September 1998 with a total value of £3.9M.

BSEP Phase 5

BBSRC made an additional tranche of funding available for this programme in 2001, and requested applications on novel aspects of the TSEs, particularly in the following priority topics:

- the nature of the infectious agent
- the normal function and structural biology of the prion protein
- molecular methods of strain differentiation
- molecular mechanisms and genetics of pathogenesis of both the CNS and PNS
- approaches underpinning the development of therapeutics
- epidemiology and modelling to underpin scrapie control
- scrapie as a natural disease model in the target species
- establishing whether PrP^{Sc} is present in sub-clinical animals

Applications from researchers new to the TSE field were particularly encouraged, as well as innovative, collaborative research proposals between centres with well-established expertise in TSE research, or between such centres and other groups with complementary expertise. Nine grants were awarded in this round with a total value of £3.5M.

TSE Diagnostics (BSD)

The development of new diagnostics tests is also a national priority. This was addressed through a

separate, joint call in 2001 by the Department of Health, Defra, BBSRC, MRC and the Food Standards Agency (FSA). Following that call, four grants were funded by BBSRC in 2002 totalling just over £1M.

Other BBSRC funding for TSE research

Since the diagnostics calls, no further phases of BSEP have been planned, but biology of the TSEs has been highlighted as one of BBSRC's cross-committee priority areas for responsive mode applications. This has not stimulated a large number of proposals to date, and eight TSE research grants have been awarded through the responsive mode committees since 2002 (average annual spend around £300k in total for these grants).

In addition, two projects (three grants) were funded under the Proteomics and Cell Function initiative (grants running between 2004–09), several grants for large equipment have been awarded for work wholly or partly on TSE research, and two BBSRC fellowships have been awarded to TSE researchers.

BBSRC has also supported TSE research for many years through core funding of a TSE research programme at the Institute for Animal Health, both at the Neuropathogenesis Unit in Edinburgh and at the Compton Laboratory. Annual spend has been between £1M and £1.5M since 2001-02.

Since 2002, seven BBSRC research studentships have been awarded for research on TSE topics.

APPENDIX 3.

GRANTS FUNDED UNDER PHASES 3 AND 4 OF BSEP

Phase 3

PI	Grant No.	Title
Brockes J	BS3 08131	Propagation of the PrP transition in cultured neural cells
Cheetham M E	BS3 08143	Chaperone interactions with PrP
Dodson G G	BS3 08136	Structural studies on prion proteins and related molecules
Fersht A R	BS3 08142	In vitro study of yeast prion structure, stability and folding
Hunter N	BS3 09722	Pathogenesis of scrapie in sheep
James W S	BS3 09665	RNA aptamers against disease isoform bovine prion protein
MacPherson G	BS3 08133	Mechanisms of transmission of TSE agents from the intestine to lymphoid tissues
McConnell I	BS3 10920	The role of the lymphoreticular system (LRS) in the replication of scrapie in genetically susceptible and resistant sheep
McLean A R	BS3 09857	Epidemiology of scrapie in sheep
Minson A C	BS3 08132	Long-term expression of mutant PrP in the murine nervous system using a viral vector
Morris R	BS3 08137	Membrane trafficking and expression of prion protein: their role in TSE
Taylor D M	BS3 08138	Partially inactivated scrapie agent as a model for the species-barrier
Young J R	BS3 08134	Bacteriophage display antibodies recognising PrP

Phase 4

PI	Grant No.	Title
Bruce M E	BS4 10558	Investigation of scrapie pathogenesis in the lymphoreticular system using in vivo germinal centre cultivation as a model system
Bruce M E	BS4 10559	Scrapie strain influences on the cellular targeting of infection in the peripheral lymphoid system
Clinton M	BS4 10547	Molecular characterisation of the pathogenesis of TSE infection
Compston A	BS4 10551	Prion protein function and neurodegeneration in a prion disease model
Dodson G G	BS4 10570	Spectroscopic, genetic and structural studies on bacterial rPrPc
Fazakerley J K	BS4 10534	Molecular analysis of neuropathological changes in a mouse model of scrapie
Fraser J R	BS4 10537	The relationship between neuron damage and clinical disease: relating murine and ovine scrapie to BSE and CJD
Hooper N M	BS4 10549	The role of the prion protein in copper metabolism
Hope J	BS4 10561	Characterisation of the N-linked glycans of the prion protein by HPLC/mass spectrometry
Hopkins J	BS4 10569	Role of lymph-borne cells in the early stages of scrapie agent replication
Hunter N	BS4 10563	PrPSc glycoform analysis and the origins of natural TSE strains in sheep
MacLeod N K	BS4 10546	Development and application of an antisense based system to study the biological function of PrP in the hippocampus
MacLeod NK	BS4 10554	The role of calcium and voltage- and calcium-gated potassium channels in TSE-related apoptotic cell death
Manson J C	BS4 10573	Alterations in TSE susceptibility defined by specific mutations in PrP
McBride P	BS4 10572	Oral TSE pathogenesis: identification of neuroanatomical pathways and interaction with lymphoid tissue
McLean A R	BS4 10539	Scrapie control by cull and selective breeding: a randomised controlled trial

APPENDIX 4.

QUESTIONNAIRE RESULTS AND ANALYSIS

SUMMARY

1. In April 2005, questionnaires were sent to 24 Principal Investigators (PIs) in receipt of 29 grants in Phases 3 and 4 of BSEP. The analysis is based on the 18 responses received, covering 21 grants.
2. 28% of PIs had previously received funding under Phases 1 and 2 and 22% had received funding via BBSRC responsive mode (for TSE and/or other research). 78% of PIs were already working in the TSEs field, with 11% completely new to the subject (pages 22-23).
3. Outputs (pages 23-25; Outputs Table pages 30-31):
 - 91 refereed papers were published from the programme (3.1 papers per grant)
 - 22% of respondents developed new tools and resources
 - 28% deposited resources in the TSE Resource Centre
 - 44% used resources held by the Centre
 - 44% reported that their research had contributed to the 3Rs
 - 56% reported membership of TSE policy committees
 - 33% took part in activities to enhance public engagement with their science
 - 31 members of staff were employed on 17 of the grants.
4. 89% of respondents reported new or improved contacts and collaborations, mostly with academic partners both in the UK and overseas (page 25).
5. 94% of respondents attended at least one of the Joint Funders' TSE Workshops, with most finding them useful (page 26).
6. 78% of respondents have applied for follow-up funding for their research, 93% of whom were successful (page 27; Outputs Table pages 30-31).
7. PIs thought that five of the six aims of the programme had been successfully met (pages 27-28).
8. 68% of respondents reported that their project had been successful in meeting its original aims. 94% reported that the grant had supported their wider research aims, with most stating that it had enabled extension of their research into new areas, and had strengthened the standing of their research group in the field (page 28).
9. 62% of respondents said there was added value to them in being part of a programme although the other 38% felt that they would have made the same progress with responsive mode funding (page 29).

Introduction

1. Questionnaires were sent to the 24 PIs in receipt of 29 grants under Phases 3 and 4 of the programme (5 PIs received two grants). The questionnaire is reproduced at Annex 5 on pages 42-45.
2. The following analysis is based on the responses received from 18 PIs, representing 21 grants, a response rate of 75% of PIs and 72% of grants. Several of those PIs in receipt of more than one grant sent a combined response, so in most cases the results are presented per PI, rather than per grant.
3. An additional grant was awarded for the establishment of the TSE Resource Centre at the Institute for Animal Health, and not for a specific research project. The PI retired during the period of the grant, and the running of the Centre was taken over by the IAH division responsible for scientific services. A progress report for the Resource Centre was submitted; this is reproduced at Annex 2 on page 32.

Questionnaire responses

- 1. Please indicate which funding bodies you held grants from at the time of applying to BSEP.**

PIs reported that they had received previous funding as follows:

Source	Number	% of all respondents
BBSRC - responsive mode	4	22
BBSRC - BSEP phases 1/2	5	28
MAFF/Defra	4	22
Department of Health	3	17
EU	6	33
MRC	8	44
Multiple Sclerosis Society	1	6
Wellcome Trust	4	22

- 2. Please give details of any industrial funding that you received for this grant.**

No respondents reported that they were in receipt of industrial funding.

- 3. How long have you been working on TSEs?**

Responses are shown in the following table. The highest proportion of respondents had been working on TSEs for between 5 and 10 years, although two said they were completely new to the subject area. One respondent has been working in this area for 19 years.

	Number	% of all respondents
<5 years	2	11
5-10 years	10	56
>10 years	6	33

4. Did you need to alter the direction of your research to fit the remit of the BSE programme?

14 PIs (78%) did not need to alter the direction of their research to fit the remit of this programme as they were already working in the field. However, 4 PIs (22%), two of whom were completely new to the TSE field, said it had been necessary.

	4 (substantially)	3	2	1 (not at all)
Number	2	2	9	5
% of all respondents	11	11	50	28

Outputs and outcomes

PIs were asked to provide details of research outputs arising as a direct result of the BSEP research grant:

5. Publications: list all papers published in refereed journals, major conference papers, book chapters and articles in popular magazines.

A total of 97 refereed papers were reported by PIs as being published from this initiative. However, 6 of these papers were joint with other BSEP PIs. Allowing for these duplicates, 91 individual papers have resulted from the initiative (3.1 papers per grant). This figure is likely to be an underestimate, however, as the list has been compiled from information in the final report forms for all projects, plus additional information for only those PIs who returned the questionnaire. The number of publications published by each PI is given in the Outputs Table on pages 30-31, and a complete list by author is given in Annex 4 (pages 35-41).

Refereed papers were published in 50 different journals, with the highest number (10 papers) being published in the Journal of General Virology.

Distribution of papers by year:

1999	2000	2001	2002	2003	2004	2005
16	22	17	27	8	6	1

Respondents have also published 6 book chapters, and presented a large number of conference presentations and abstracts.

6. Other outputs:

Respondents were asked to give details of any other outputs arising from the grant.

Four PIs (22%) reported the development of new tools and resources, as follows:

- Novel techniques for examining TSE pathology
- Sheep cytokine RNAase protection assay
- Cell based DELFIA assay for PrP^c
- Specialised constructs involving the N-terminus of PrP, and antibodies.

Five respondents (28%) had deposited resources in one of the TSE resource centres, although more (8: 44%) had actually used resources from them. Full details of the resources deposited and used are given below.

Resources: give details of any resources that you deposited in: 1. IAH TSE Resource Centre 2. VLA Tissue Bank 3. NIBSC CJD Resource Centre 4. NCJDSU Tissue Bank	<ul style="list-style-type: none"> • Atomic parameters of sheep 123-231 prion construct (PDB) • Blocks and sections (NPU archive) • Aliquots of recombinant protein (distributed through IAH TSERC) • Sheep tissues submitted to VLA tissue bank, but also many tissues have been supplied directly to other laboratories both in the UK and Europe • Mice and tissues have been supplied to many laboratories throughout the world
Use of resources: give details of any resources that you used from the resource centres above.	<ul style="list-style-type: none"> • Scrapie infected mouse brains as source of infectivity from IAH • Blood samples from NPU, VLA, NCJDSU • Antibodies from VLA, and IAH TSERC • Access to tissues and sheep from VLA; antibodies and PrP proteins from IAH TSERC • Original PrP expression construct from IAH TSERC

Two PIs have applied for a patent. Eight respondents (44%) reported that their research project had contributed to the replacement, reduction or refinement of animals in experiments. Two of these involved the use of *in vitro* techniques which reduced the number of animals being used. Other contributions to the 3Rs included:

- new culture systems for analysing transfer of infectivity as an alternative to animal experimentation
- targeting which genotypes of sheep are required for future experiments, allowing omission of others
- cell lines developed from sheep are used in gene expression studies to avoid carrying out exploratory studies in sheep themselves
- only natural scrapie cases used; no additional experimental animals used
- cannulated sheep are now kept in floor pens rather than metabolism crates
- lowest species used (mouse).

Ten respondents (56%) reported membership of TSE policy committees, such as SEAC, HSE, MAFF/Defra, Royal Society, MRC, WHO, and EU. One respondent has had considerable involvement in both national and international TSE committees.

Six PIs (33%) have taken part in activities to enhance public engagement with their science, including open days, public talks, media interactions, and displays at the Royal Show and other agricultural shows.

Details of outputs by each PI are given in the Outputs Table on pages 30-31.

7. Staff: provide details of all staff employed on the grant.

Thirty one staff were employed on 17 of the grants in the following grades:

On appointment		Prior to appointment	
Grade	No.	Grade	No.
RA	11	RA	9
Post-doc	7	Undergraduate	2
PhD student	1	PhD student	12
IAH/NPU staff	10	IAH/NPU staff	4
Technician	2	Technician	4

On completion of their employment on the grant, their first destinations were as follows:

Destination	UK	Overseas
Academia/research institute*	16	5
Industry - research	4	1
Industry (sales)	1	
Government	1	1
Charity - research	1	
Other (world travel)		1

*includes those remaining in the same laboratory

Details of the number of staff employed on each grant are given in the Outputs Table on pages 30-31.

Networking and collaboration

8. One of the aims of the programme was to encourage networking and collaboration within the TSE community. Please give details of any new or improved contacts or collaborations, and comment on the impact that they had on the progress of your research.

All except two respondents (16: 89%) reported improved contacts and collaborations through participating in the programme, mostly with academic partners both in the UK and overseas. There were increased collaborations between UK university-based researchers and institute-based researchers at IAH.

Some respondents commented that they already collaborated with others in the field in the UK, but that participation in the programme had increased the number of international collaborations. The overseas collaborations were with academic institutions in Germany, France, Ireland, The Netherlands, US, Japan and China, several of which have already resulted in joint publications and/or grant funding.

There were two industrial contacts established, with Perkin-Elmer and Biogenesis (one in the UK and one overseas).

Summary: number of contacts and collaborations:

New or improved academic contacts	UK	15
	Overseas	10
New or improved industrial contacts	UK	1
	Overseas	1
New formal academic research collaboration (e.g. joint publication, joint funding application)	UK	9
	Overseas	9
New formal industrial research collaboration (e.g. joint publication, joint funding application)	UK	
	Overseas	1

One respondent from King's College London reported that they had set up a monthly forum at Guy's Hospital to provide the opportunity for discussion and collaboration for those who were new to the field and were interested in the cell biological aspects of prion disease. Membership of the group has changed over the years but, as well as those based in London, researchers from Oxford, Cambridge and IAH have also attended. The meetings have resulted in many useful informal exchanges plus major cross-disciplinary collaborations with researchers in Manchester and Warwick.

9. Did you or a member of your group attend the Joint Funders' TSE workshops?

17 respondents (94%) attended at least one workshop. The other PI did not attend any but was represented by a colleague at one of them. Attendance was as follows:

Date	Location	Number of PIs attending	Number of others attending
1998	Warwick	13	7
2000	Keele	15	9
2002	Durham	14	10
2004	York	12	11

If yes, how useful were they?

Date	Location	Number reporting that they were:		
		Useful	Interesting but not useful	Neither interesting nor useful
1998	Warwick	12	4	1
2000	Keele	12	2	4
2002	Durham	13	2	3
2004	York	15	1	

10. Do you have any suggestions for how the workshops could be improved?

Seven respondents commented on the workshops, as follows:

- there was too much politics in the Joint Funders' meetings; which seemed to intrude on the normal conduct of a scientific meeting in terms of selection of speakers, organisation and atmosphere
- more presentations should have been selected from the posters
- the choice of keynote speakers was not always appropriate - younger speakers would have made the workshops more dynamic. The well-respected figures tended to give review lectures rather than presenting new data (possibly because the workshops were not regarded as a prestigious place to present the latest data) so they did not come across as well as they might have
- the format was very good, but it would have been good to have more time to review the posters and discuss them in conference
- given the scope, you will always get complaints, since the basic science is not appreciated by all those working on more applied aspects and *vice versa*
- the workshops became less useful when policy and funding were also discussed - the scientific discussions became less productive as the numbers attending increased. A return to the smaller groups of people as at the Warwick meeting would help interactions between groups
- nice surroundings and good accommodation really help with networking, but some of the venues were depressing. The poster facilities at York were excellent.

Funding

11. Please give details of any applications that you have made for funding to continue or develop the work funded by the BSEP grant.

14 respondents (78%) have applied for follow-up funding, 13 of whom (93%) were successful. Some of these also said that they will be applying for additional funding in future. Details of funding gained are given in the Outputs Table on pages 30-31.

Source	No. of applications	No. funded
BBSRC responsive mode	4	2
BBSRC BSEP	8	6
Defra	1	1
Department of Health	3	3
EU	4	4
FSA	2	1
MRC	6	4
Other*	5	5

*Chinese Academy of Sciences, Natural Science Foundation of China, and Ministry of Science and Technology of China.

In addition, one IAH respondent commented that, although their application for a follow-up BSEP grant was unsuccessful, their BBSRC core funding had been increased. Another was unable to answer the question as they had not kept any records.

12. If you have not yet applied for funding to continue or develop the work funded by the BSEP grant, are you planning to do so?

Of the remaining two respondents, one is currently considering the future direction of their research and may apply for follow-up funding; the other has decided to stop work in the TSE area and to concentrate on their other research interests.

Aims and objectives

13. Do you think the programme was successful in meeting its aims?

Five of the aims were thought to have been successfully met, with respondents mainly selecting options 4 and 3. However, the aim of ensuring full exploitation of skills and expertise was thought to have been less successful. Not all respondents commented on every aim, so the percentages are calculated according to the total number that replied to each one, as follows.

	No. of replies received	4 very successful	3	2	1 not successful
Encourage molecular, genetic, cellular and functional approaches to elucidating mechanisms of TSE transmission, PrP conversion and replication	16	4 (25%)	11 (69%)	1 (6%)	
Understand more about the molecular structure and function of prion proteins, including the biological function of normal PrP	16	3 (19%)	7 (44%)	5 (31%)	1 (6%)
Understand more about pathogenesis and disease progression, to promote rational approaches to intervention	16	2 (13%)	10 (63%)	4 (25%)	

Ensure full exploitation of the body of skills and expertise that had been built up	15	3 (20%)	3 (20%)	8 (53%)	1 (7%)
Encourage innovative research involving collaboration between centres with well-established expertise in TSE research	16	2 (13%)	8 (50%)	4 (25%)	2 (13%)
Encourage collaboration between such centres and other groups with complementary expertise that were able to bring new approaches to bear on the important questions.	15	4 (27%)	6 (40%)	4 (27%)	1 (7%)

14. Was your own project successful in meeting its original objectives?

Responses were received from 18 PIs, representing 19 individual grants. Thirteen of these (68%) reported that they were successful in meeting their original objectives, although 6 respondents reported that their projects were less successful. Responses were as follows:

4 (very successful)	3	2	1 (not successful)
6 (32%)	7 (37%)	6 (32%)	-

The 6 respondents who selected option 2 above gave the following reasons:

	1	2	3	4	5	6
Staff, e.g. difficulties in recruiting and retaining staff		✓				
Experimental/methodological/technical reasons	✓		✓	✓		
Lack of resources, e.g. funding, equipment, facilities	✓		✓			
Insufficient time to complete experiments	✓	✓	✓			✓
Other (difficulties of meeting safety requirements; laboratory was flooded and research time was lost)					✓	✓

15. Did this grant support your wider research aims?

17 respondents (94%) confirmed that participation in the BSEP initiative had supported their wider research aims. Of the 17 PIs who replied to this question, the largest proportion (15: 88%) reported that it had enabled extension of their research into new areas. Fourteen respondents (82%) reported that it had strengthened the standing of their research group in the field: one commented that it had significantly enhanced the careers of all 3 members of staff on the grant; and another commented that the grant had established the research group in the TSE area. Responses were as follows:

	No. of PIs	% of those who replied
Enabled extension of your research into new areas	15	88
Provided funding for activities that other bodies would not fund	4	24
Strengthened the skill base of the group, e.g. techniques, cross-disciplinary skills	12	71
Helped to publicise the importance of your field of research	6	35
Strengthened the standing of your research group in the field	14	82
Contributed to maintenance/development/purchase of equipment/facilities	6	35
Contributed to the development of tools, technologies, or reagents	8	47
Enhanced the progress of your career	9	53

16. Was there any added value to you in being part of a programme, or do you think you would have made similar progress in your research by receiving a grant via normal responsive mode?

Of the 13 PIs who replied to this question, 8 (62%) said that there was added value to them in being part of a programme, with the remaining 5 respondents (38%) saying that they would have made similar progress with responsive mode funding. The main reason given for the added value was the interaction between groups, especially at the biennial workshops, where they could exchange ideas with colleagues; this was particularly useful for PIs who were new to the field. All comments are given in full in Annex 3 on pages 33-34.

Other

17. Do you have any comments on the management of the programme by BBSRC?

There was mostly positive feedback from respondents on the management of the programme, although one PI commented that they would have found it useful to have had a specific contact at BBSRC to discuss their project with. All comments are given in full in Annex 3 on pages 33-34.

18. Please feel free to express your views on any other aspects of the programme.

The general feeling was that the BSE Programme was important and that it had enabled a considerable amount of progress in research into the TSEs. All comments are given in full in Annex 3 on pages 33-34.

Annex 1 - Outputs table

Grant No.	Lead PI	Returned questionnaire	No. of refereed publications	Tools & resources developed	Resources		Contribution to 3Rs	Contribution to policy discussions	Public engagement activities	Trained staff	Further funding received
					Deposited	Used					
BS3 08131	Brockes J	✓	3			✓	✓	✓		2	
BS4 10558	Bruce M E										
BS4 10559	Bruce M E		6*								
BS3 08143	Cheetham M E	✓	2							3	
BS4 10547	Clinton M	✓	5			✓				1	DoH, FSA, MRC
BS4 10551	Compston A/ Brown D	✓	10				✓	✓	✓	2	DoH: £219k
BS3 08136	Dodson G G	✓	4		✓			✓		3	DoH: £650k EU: £235k
BS4 10570											
BS4 10534	Fazakerley J K	✓						✓		2	BBSRC: £198k, £897k**
BS3 08142	Fersht A R	✓	3				✓		✓	3	NSFC: total £26k *** CAS: total £34k MOST: total £3k
BS4 10537	Fraser J R	✓	3	✓	✓					1	
BS4 10549	Hooper N M	✓	4			✓			✓	1	EU: £111k MRC: £300k, £1.6M
BS4 10561	Hope J	✓	5		✓			✓		2	BBSRC: £200k
BS4 10569	Hopkins J	✓	2	✓		✓				1	BBSRC: £897k**
BS3 09722	Hunter N	✓	13		✓	✓	✓	✓	✓	4	
BS4 10563	Hunter N		4							1	
BS3 09665	James W S		1*								
BS4 10546	MacLeod N K										
BS4 10554	MacLeod N K										
BS3 08133	MacPherson G	✓	3					✓		1	EU: £150k

Grant No.	Lead PI	Returned questionnaire	No. of refereed publications	Tools & resources developed	Resources		Contribution to 3Rs	Contribution to policy discussions	Public engagement activities	Trained staff	Further funding received
					Deposited	Used					
BS4 10573	Manson J C	✓	6		✓	✓		✓		1	Defra: £315k
BS4 10572	McBride P	✓	2				✓			1	EU: £306k
BS3 10920	McConnell I	✓	1	✓			✓	✓	✓		BBSRC: £413k, £402k
BS3 09857	McLean A R	✓	15								
BS4 10539											
BS3 08132	Minson A C		1*								
BS3 08137	Morris R	✓	4	✓		✓	✓	✓	✓	2	BBSRC: £484k, £203k MRC: £306k
BS3 08138	Taylor D M										
BS3 08134	Young J R										

* data from final report only

** joint grant: Fazakerley and Hopkins

*** Natural Science Foundation of China, Chinese Academy of Sciences, and Ministry of Science and Technology of China.

Annex 2 – Report from TSE Resource Centre

The primary objective of the TSE Resource Centre (TSERC) is to collect, produce, store and distribute sought after reagents needed by publicly funded TSE researchers. Work on equipping the Centre began in May 1998 and with the successful collection and production of the first reagents, the TSERC opened to requests in April 1999. Since then the list of reagents available on request from the Centre has steadily increased and over 1550 samples have been delivered to a range of research establishments world-wide.

The TSERC has been successful in collecting, producing and characterising stocks of reagents for one of the most varied ranges of TSE specific reagents, available on request from one site. Included in the list of over thirty reagents distributed from the centre over the past six years are: Eight different monoclonal antibodies; ten types of infectious brain homogenates carrying defined rodent strains of scrapie; five control brain homogenates; five mouse strains of known Prn-p genotype; three cell lines (scrapie infected and control); pentosan sulphate; recombinant PrP. Many of these reagents are not available commercially.

The considerable interest shown by researchers in using the reagents collected and produced by the TSE Resource Centre is evident from the number of requests handled by the Centre. By the end of 2004 the TSERC had received 674 individual reagent requests and had shipped over 1550 individual samples. Over sixty publications citing the use of these TSERC reagents have been identified.

425 requests for individual TSERC reagents originated from UK researchers. The vast majority of these researchers were funded by BSEP, DEFRA, FSA, HPA, BBSRC, MRC, EU, Leverhulme or Working Group for Research on the Decontamination of Surgical Instruments. The remainder of the requests were from publicly funded centres world-wide.

Whilst Institute for Animal Health researchers have been more than generous in depositing reagents with the TSERC, the response from researchers outside the Institute has been disappointing. Despite strenuous efforts on the part of TSERC staff and the “expectation” on the part of the MRC and BBSRC that reagents generated during the course of funded work should be lodged with the TSERC, the TSERC currently distributes just one reagent donated from a non-IAH source. It would appear that not all scientists subscribe to the view that, even when published, a reagent should be made freely available to other researchers. The “expectation” on the part of Funders that those funded will make available reagents is just too weak.

In summary, the ISO 9001:2000 accredited TSERC is now a well-established resource, playing a role complementary to that of the TSE Archive at the Veterinary Laboratories Agency and the CJD Resource Centre at NIBSC, in providing sought after, cost-effective TSE reagents to researchers funded by a number of different bodies across the UK and further afield. Interest shown by researchers in the reagents currently available from the TSERC remains high, with the number of requests executed in the first quarter of 2005 being greater than all quarters in 2004.

Phil Jones
IAH, Compton Laboratory

Annex 3 - Full responses to Questions 16-18

Question 16: Was there any added value to you in being part of a programme, or do you think you would have made similar progress in your research by receiving a grant via normal responsive mode?

- One learns a lot by meeting other scientists with different techniques; the TSE biology and experimental approaches were new and interesting to me. A particular interest was fibre formation, an intractable material for structural analysis. Programmes like this one (like the Aids Directed Programme) have a valuable role in generating a scientific community. They stimulate real understanding of the scientific and, if relevant, social issues and it is where collaborations can start naturally.
- Yes, the Joint Funders meetings were extremely useful, promoting networking and collaboration.
- The programme was useful in that it encouraged interaction between groups and provided a meeting at which we could exchange ideas. I think it became less useful when the meeting also became a venue at which policy/funding was more high profile. The science discussions became less productive as the numbers attending increased. A return to smaller numbers of people would help the interactions between groups.
- We would not have made progress without the collaborations - we had no TSE experience at all.
- Yes, this is an important and specialised field where it is essential to build capacity in other labs outside IAH and VLA. To that extent the BSEP initiative is to be welcomed.
- Yes. There were a lot of us in the same predicament: well-established careers in other, highly relevant areas, wanting to get into the arcane, pressurised and hotly disputed field of TSE. We hung together through the Prion Forum and have made, and are still making, significant contributions.
- The programme encouraged proven expertise and substantial experimental resources to be applied in a new research direction.
- At the Joint Funders Conferences it did feel that 90% of the progress was being made by 10% of the groups funded by BSEP. It is likely that our work would have progressed as well in without BSEP (if we'd been successful in competitive mode funding bids!) but, from our perspective of both BSEP and TAP, I feel the Programme approach benefits UK science in general and should be encouraged. Without TAP we'd never have been in a position to compete on PrP transgenic mice and provide an independent view on prions over the years.
- The outcome would have been the same if the grant was normal response mode.
- No obvious added value, other than meeting with other researchers at the TSE Funders workshops.
- Little added value. Project could have been undertaken through other funding.

Question 17: Do you have any comments on the management of the programme by BBSRC?

- Prion research was, and is, generally difficult and in the early days I considered there was too much weight given to simple productivity in the assessment of outcomes and in grant reports. The research presented a number of problems, e.g. it needed safety standards that could inhibit and delay experiments; it often needed fairly basic techniques that did not often lead to useful publications; and it needed considerable physical biochemistry and not too many people are well qualified in this area. With structural research three year grants were more than usually difficult to work to, it was often too short to research a system when there was very

limited biology and there were practical uncertainties with preparing stable solutions suitable for NMR and for crystallization.

- I think it would have been useful to have had a contact within BBSRC with whom progress of problems with the work could have been discussed on an ongoing basis.
- Generally very good in phases 3 and 4. Phase 1 was very poorly managed and I think the research council had learnt its lessons well by Phase 3.
- It is good and I hope it can be maintained. There remains a need for the joint funders to have a single grants board.
- The BBSRC has always been a delight to work with – straightforward and uncomplicated.

Question 18: Please feel free to express your views on any other aspects of the programme.

- The BSEP Programme should be maintained and should do more to maintain the survival of prion groups (especially successful ones) outside VLA and IAH.
- There were sometimes most frustrating safety issues.
- The BBSRC first funded TSE transgenic mouse work as part of their TAP programme before the advent of BSEP. Although successful, no Tg mouse lines are currently available to other UK agencies that were produced as part of BSEP or TAP except the PrP null mouse lines produced independently by Martin Hooper and David Melton at the University of Edinburgh, in collaboration with IAH. The BBSRC should do more to encourage the interchange of these and other products of government-funded research between their institutions and other government departments such as HPA and the VLA.
- BSEP permitted an extraordinary broadening of the range of TSE research in the UK, enabling the traditional TSE centres to interact with the UK universities, introducing them to new questions and technologies.
- Because the BSE epidemic is over and the vCJD epidemic in apparent decline there may be a tendency to think that TSE science no longer needs funding. This would be extremely short sighted. As a consequence of the considerable R and D investment several things have happened:
 - There is an enlarged skill base in TSE research
 - Reagents and model systems have been developed (but need to be better shared)
 - New aspects especially in pathogenesis of naturally occurring TSE diseases are emerging
 - Atypical scrapie strains and BARBS need to be understood. Other animal TSEs are increasingly being recognised
 - Transgenic models are much improved
 - There is a greatly enlarged and enthusiastic scientific community who are fascinated by the TSEs and this is growing outside the two major centres of VLA and IAH
 - TSE research may well provide the best route into study of neurodegenerative diseases generally and TSE research needs to be viewed in the wider context of neuroscience and not just as a unique (and past) episode in diseases of animals and man. By way of analogy the long term R and D effort in basic immunology and retroviruses long before the discovery of the AIDS virus proved to have provided a wealth of information and powerful research base of immediate application to understanding immunodeficiency viruses in animals and man when they arrived. TSE research may be analogous to this and has provided the research capacity to investigate neurodegenerative diseases in greater depth. The lessons from TSE research may impact on Alzheimers research.

Annex 4 - publications in refereed journals

This list has been compiled using information in final report forms for all projects, plus additional updated information for the 18 PIs who returned the questionnaire.

Professor J Brockes - BS3 08131

Brockes, J.P. (1999) Topics in prion cell biology, *Current Opinion in Neurobiology*, **9**, 571-577.

Kanu, N., Drechsel, D.N., Imokawa, Y., Williamson, R.A., Birkett, C.R., Bostock, C.J. and Brockes, J.P. (2002) Transfer of scrapie prion infectivity by cell contact in culture. *Current Biology*, **12**, 523-30.

Moroncini, G., Kanu, N., Solforosi, L., Abalos, G., Telling, G.C., Head, M., Ironside, J., Brockes, J.P., Burton, D.R. and Williamson, A.R. (2004) Motif-grafted antibodies containing the replicative interface of cellular PrP are specific for PrP^{Sc}. *Proceedings of the National Academy of Sciences of the United States of America*, **101**, 10404-10409.

Dr M E Bruce - BS4 10559

Brown, K.L., Stewart, K., Ritchie, D.L., Mabbott, N.A., Williams, A., Fraser, H., Morrison, W.I. and Bruce, M.E. (1999) Scrapie replication in lymphoid tissues depends on prion protein expressing follicular dendritic cells. *Nature Medicine*, **5**, 1308-1312.

Ritchie, D.L., Brown, K.L. and Bruce, M.E. (1999) Visualisation of PrP protein and follicular dendritic cells in uninfected and scrapie infected spleen. *Journal of Cellular Pathology*, **1**, 3-10.

Brown, K.L., Ritchie, D.L., McBride, P.A. and Bruce, M.E. (2000) The detection of PrP in extraneural tissues. *Microscopy Research and Technique*, **50**, 40-45.

Brown, K.L., Stewart, K., Ritchie, D., Fraser, H., Morrison, W.I. and Bruce, M.E. (2000) Follicular dendritic cells in scrapie pathogenesis. *Archives of Virology*, **16**, 13-21.

Bruce, M.E., Brown, K.L., Mabbott, N.A., Farquhar, C.F. and Jeffrey, M. (2000) Follicular dendritic cells in TSE pathogenesis. *Immunology Today*, **21**, 442-446.

Jeffrey, M., McGovern, G., Goodsir, C.M., Brown, K.L. and Bruce, M.E. (2000) Sites of prion protein accumulation in scrapie-infected mouse spleen revealed by immuno-electron microscopy. *Journal of Pathology*, **191**, 323-332.

Professor M E Cheetham - BS3 08143

Chapple, J.P. and Cheetham, M.E. (2003). The chaperone environment at the cytoplasmic face of the endoplasmic reticulum can modulate rhodopsin processing and inclusion formation. *Journal of Biological Chemistry*, **278**, 19087-19094.

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Dr M Clinton - BS4 10547

Miele, G., Slee, R., Manson, J. and Clinton, M. (1999) A rapid protocol for the authentication of isolated differential display RT-PCR CDNAs. *Preparative Biochemistry and Biotechnology*, **29**, 245-255.

Clinton, M., Manson, J., McBride, D. and Miele, G. (2000) Gene expression changes during murine postnatal brain development. *Genome Biology*, **1**, RESEARCH0005. Epub 2000 Sep01.

Miele, G., Manson, J. and Clinton, M. (2001) A novel erythroid-specific marker of transmissible spongiform encephalopathies. *Nature Medicine*, **7**, 361-364.

Miele, G., Jeffrey, M., Turnbull, D., Manson, J. and Clinton, M. (2002) Ablation of cellular prion protein expression affects mitochondrial numbers and morphology. *Biochemical and Biophysical Research Communications*, **291**, 372-377.

Miele, G., Alejo Blanco, A.R., Baybutt, H., Horvat, S., Manson, J. and Clinton, M. (2003) Embryonic activation and developmental expression of the murine prion protein gene. *Gene Expression*, **11**, 1-12.

Professor A Compston/Professor D R Brown - BS 10551

Brown, D.R. (1999) Prion protein peptide neurotoxicity can be mediated by astrocytes. *Journal of Neurochemistry*, **73**, 1105-1113.

McHattie, S.J., Brown, D.R. and Bird, M.M. (1999) Cellular uptake of the prion protein fragment PrP106-126 in vitro. *Journal of Neurocytology*, **28**, 145-155.

Burkle, A., Kretzschmar, H.A. and Brown, D.R. (1999) Poly(ADP-ribose) immunostaining to detect apoptosis induced by a neurotoxic fragment of prion protein. *Histochemical Journal*, **31**, 711-716.

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Brown, D.R., Clive, C. and Haswell, S.J. (2001) Anti-oxidant activity related to copper binding of native prion protein. *Journal of Neurochemistry*, **76**, 69-76.

Professor G G Dodson - BS3 08136, BS4 10570

Gill, A.C., Ritchie, M.A., Hunt, L.G., Steane, S.E., Davies, K.G., Bocking, S.P., Rhie, A.G., Bennett, A.D. and Hope, J.A. (2000) Post-translational hydroxylation at the N-terminus of the prion protein reveals presence of PPII structure in vivo. *EMBO Journal*, **19**, 5324-31.

Riley, M.L., Leucht, C., Gauczynski, S., Hundt, C., Brecelj, M., Dodson, G. and Weiss, S. (2002) High-level expression and characterization of a glycosylated covalently linked dimer of the prion protein. *Protein Engineering*, **15**, 529-536.

Whyte, S.M., Sylvester, I.D., Martin, S.R., Gill, A.C., Wopfner, F., Schatzl, H.M., Dodson, G.G. and Bayley, P.M. (2003) Stability and conformational properties of doppel, a prion-like protein, and its single-disulphide mutant. *Biochemical Journal*, **373**, 485-494.

Haire, L.F., Whyte, S.M., Vasisht, N., Gill, A.C., Verma, C., Dodson, E.J., Dodson, G.G. and Bayley, P.M. (2004) The crystal structure of the globular domain of sheep prion protein. *Journal of Molecular Biology*, **336**, 1175-83.

Professor Sir Alan Fersht - BS3 08142

Perrett, S., Freeman, S.J., Butler, P.J. and Fersht, A.R. (1999) Equilibrium folding properties of the yeast prion protein determinant Ure2. *Journal of Molecular Biology*, **290**, 331-345.

Zhou, J.M., Zhu, L., Balny, C. and Perrett, S. (2001) Pressure denaturation of the yeast prion protein Ure2. *Biochemical and Biophysical Research Communications*, **287**, 147-152.

Galani, D., Fersht, A.R. and Perrett, S. (2002) Folding of the yeast prion protein Ure2: kinetic evidence for folding and unfolding intermediates. *Journal of Molecular Biology*, **315**, 213-227.

Dr J R Fraser - BS4 10537

Jamieson, E., Jeffrey, M., Ironside, J.W. and Fraser, J.R. (2001) Apoptosis and dendritic dysfunction precede prion protein accumulation in 87V scrapie. *NeuroReport*, **12**, 2147-2153.

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Fraser, J.R. (2002) What is the basis of TSE induced neurodegeneration, and can it be repaired? *Neuropathology and Applied Neurobiology*, **28**, 1-11.

Professor N M Hooper - BS4 10549

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Hooper, N.M. (2002) Prion disease: close encounters of the cellular kind. *Current Biology*, **12**, R248-249.

Dr J Hope - BS4 10561

Brimacombe, D., Bennett, A., Wusteman, F., Gill, A. and Bostock, C. (1999) Characterisation and polyanion binding properties of purified recombinant prion protein. *Biochemical Journal*, **342**, 605-613.

Stimson, E., Hope, J., Chong, A. and Burlingame, A.L. (1999) Site-specific characterization of the N-linked glycans of murine prion protein by high-performance liquid chromatography/electrospray mass spectrometry and exoglycoside digestions. *Biochemistry*, **38**, 4885-4895.

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Ritchie, M.A., Deery, M.J., Lilley, K. and Gill, A.C. (2002) Precursor ion scanning for detection and structural characterization of heterogeneous glycopeptide mixtures. *Journal of the American Society for Mass Spectrometry*, **13**, 1065-1077.

Professor J Hopkins - BS4 10569

Hopkins, J. (2002) Molecular immunology-gene regulation and signal transduction. *Veterinary Immunology and Immunopathology*, **87**, 245-249.

Gossner, A.G., Watkins, C., Bailey, S., Hunter, N. and Hopkins, J. (2002) Patterns of cytokine gene expression of naïve and memory T lymphocytes. *Veterinary Immunology and Immunopathology*, **87**, 261-264.

Dr N Hunter - BS3 09722

Baylis, M., Houston, F., Goldmann, W., Hunter, N. and McLean, A.R. (2000) The signature of scrapie: differences in the PrP genotype profile of scrapie-affected and scrapie-free UK sheep flocks. *Proceedings of the Royal Society (London) Series B*, **267**, 2029-2035.

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Barclay, G.R., Houston, E.F., Halliday, S.I., Farquhar, C.F. and Turner, M.L. (2002) Comparative analysis of normal prion protein expression on human, rodent and ruminant blood cells by using a panel of prion antibodies. *Transfusion*, **42**, 517-526.

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Davies, M.L., Hopkins, L.J., Halliday, S., Houston, F., Hunter, N. and McConnell, I. (2004) Architecture of secondary lymphoid tissue in sheep experimentally challenged with scrapie. *Immunology*, **111**, 230-236.

Dr N Hunter - BS4 10563

Houston, F., Foster, J.D., Chong, A., Hunter, N. and Bostock, C.J. (2000) Transmission of BSE by blood transfusion in sheep. *The Lancet*, **356**, 999-1000.

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Dr W S James - BS3 09665

James, W.S. (2001) Nucleic acid and polypeptide aptamers: a powerful approach to ligand discovery. *Current Opinion in Pharmacology*, **1**, 540-546.

Dr G MacPherson - BS3 08133

Huang, F.P. and MacPherson, G.G. (2001) Continuing education of the immune system-dendritic cells, immune regulation and tolerance. *Current Molecular Medicine*, **1**, 457-468.

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Dr J C Manson - BS4 10573

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Professor P A McBride - BS4 10572

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Professor I McConnell - BS3 10920

Davies, M.L., Hopkins, L.J., Halliday, S., Houston, F., Hunter, N., and McConnell, I. (2004) Architecture of secondary lymphoid tissue in sheep experimentally challenged with scrapie. *Immunology*, **111**, 230-236.

Professor A R McLean - BS3 09857, BS4 10539

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Professor A C Minson - BS3 08132

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Professor R Morris - BS3 08137

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Annex 5 - Questionnaire

Evaluation of Biology of Spongiform Encephalopathies Programme (BSEP) Phases 3 and 4

Questionnaire

Name of Principal Investigator:

Institution:

Grant No:

Title:

1. Please indicate which funding bodies you held grants from at the time of applying to BSEP. (please tick)

BBSRC - responsive mode		FSA	
BBSRC - BSEP		Industry ¹	
MAFF/Defra		MRC	
Department of Health		Wellcome Trust	
EU		Other ²	

¹ please give company name

² please specify

2. Please give details of any industrial funding that you received for this BSEP grant.

Source	Value (£)

3. How long have you been working on TSEs? (please tick)

<5 years	5-10 years	>10 years

4. Did you need to alter the direction of your research to fit the remit of the BSE programme? (please tick one box)

4 (substantially)	3	2	1 (not at all)

Please give details.

Outputs and outcomes

Please provide details of research outputs arising as a direct result of the BSEP research grant:

5. **Publications:** list all papers published in refereed journals, major conference papers, book chapters and articles in popular magazines. Please highlight co-authors from **industry** or from overseas.

6. **Other outputs:** (please give details)

Tools and resources: any new tools or resources that were developed from the grant	
Resources: give details of any resources that you deposited in: 1. IAH TSE Resource Centre 2. VLA Tissue Bank 3. NIBSC CJD Resource Centre 4. NCJDSU tissue bank. If none, please give reasons.	
Use of resources: give details of any resources that you used from the resource centres above.	
IP: patents, licences, etc: details of any patents applied for/granted, licences/options executed from IP arising from the grant	
Contribution to the 3Rs: contribution to the replacement, reduction or refinement of animals in experiments	
Contribution to policy discussions: e.g. membership of advisory committees and/or working groups related to TSEs	
Participation in activities to enhance public engagement with the biosciences.	

7. **Staff:** provide details of all staff employed on the grant.

Name	Grade/position	Period of appointment	Previous position before BSEP	First destination after BSEP

Networking and collaboration

8. One of the aims of the programme was to encourage networking and collaboration within the TSE community. Please give details of any new or improved contacts or collaborations, and comment on the impact that they had on the progress of your research:

New or improved academic contacts - <i>if cross-disciplinary, please specify which discipline</i>	UK	
	Overseas	
New or improved industrial contacts - <i>please specify type of industry</i>	UK	
	Overseas	
New formal academic research collaboration (e.g. joint publication, joint funding application) - <i>if cross-disciplinary, please specify which discipline</i>	UK	
	Overseas	
New formal industrial research collaboration (e.g. joint publication, joint funding application) - <i>please specify type of industry, nature of collaboration</i>	UK	
	Overseas	

Comments:

9. Did you or a member of your group attend the following Joint Funders' TSE workshops? If yes, how useful were they? (please tick)

Date	Location	PI	Others	Useful	Interesting but not useful	Neither interesting nor useful
1998	Warwick					
2000	Keele					
2002	Durham					
2004	York					

10. Do you have any suggestions for how the workshops could be improved?

Funding

11. Please give details of any applications that you have made for funding to continue or develop the work funded by the BSEP grant.

Source	Year applied	Grant reference no/ application title	Funded Y/N	Value (£)	Period of grant
BBSRC					
Defra					
Department of Health					
EU					
FSA					
Industry ¹					
MRC					
Wellcome Trust					
Other ²					

¹ please give company name

² please specify

12. If you have not yet applied for funding to continue or develop the work funded by the BSEP grant, are you planning to do so? Yes/No
Please give details

Aims and objectives

13. Do you think the programme was successful in meeting its aims? (please tick)
The aims were to build on the findings from phases 1 and 2, and to:

	4 (very successful)	3	2	1 (not successful)
Encourage molecular, genetic, cellular and functional approaches to elucidating mechanisms of TSE transmission, PrP conversion and replication				
Understand more about the molecular structure and function of prion proteins, including the biological function of normal PrP				
Understand more about pathogenesis and disease progression, to promote rational approaches to intervention				

Ensure full exploitation of the body of skills and expertise that had been built up				
Encourage innovative research involving collaboration between centres with well-established expertise in TSE research				
Encourage collaboration between such centres and other groups with complementary expertise that were able to bring new approaches to bear on the important questions.				

14. Was your own project successful in meeting its original objectives?

4 (very successful)	3	2	1 (not successful)

If you ticked 1 or 2, were the reasons for this related to:

Staff, e.g. difficulties in recruiting and retaining staff	
Experimental/methodological/technical reasons	
Lack of resources, e.g. funding, equipment, facilities	
Insufficient time to complete experiments	
Other, please specify	

Comments:

15. Did this grant support your wider research aims? (please tick one or more boxes and comment if you wish)

Enabled extension of your research into new areas	
Provided funding for activities that other bodies would not fund	
Strengthened the skill base of the group, e.g. techniques, cross-disciplinary skills	
Helped to publicise the importance of your field of research	
Strengthened the standing of your research group in the field	
Contributed to maintenance/development/purchase of equipment/facilities	
Contributed to the development of tools, technologies, or reagents	
Enhanced the progress of your career	
Other (<i>please specify</i>)	

Comments:

16. Was there any added value to you in being part of a programme, or do you think you would have made similar progress in your research by receiving a grant via normal responsive mode?

Please give details.

Other

17. Do you have any comments on the management of the programme by BBSRC?

18. Please feel free to express your views on any other aspects of the programme.