

Evaluation of Phases 3 and 4 of the BBSRC Biology of the Spongiform Encephalopathies Programme

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This document presents the conclusions of a review panel of experts in this field.
The views expressed are entirely those of the members of the panel.

BBSRC
Polaris House
North Star Avenue
Swindon
SN2 1UH
www.bbsrc.ac.uk

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EXECUTIVE SUMMARY AND KEY CONCLUSIONS

This document sets out the views of a review panel convened to provide an independent evaluation of phases 3 and 4 of the BBSRC Biology of the Spongiform Encephalopathies Programme (BSEP).

The panel was asked to consider:

- the extent to which the scientific and general objectives of the programme were met
- the overall quality of the research, as informed by an analysis of final reports
- the major outputs and outcomes, as informed by a survey of grantholders
- the extent to which the programme met the policy needs of other funders in the TSE field
- the added value of funding this research as a directed programme

The overall conclusion of the panel was that the research funded in BSEP phases 3 and 4 was important and had provided valuable scientific insights, although only a small number of projects had produced outstanding results that had underpinned subsequent research and policy development. The research compared well with similar research being carried out in Europe and the US although, given the opportunities in the UK, it would be disappointing were this not so.

Research quality (pages 7-8)

A small number of grants had produced excellent results and had met all their objectives; others had been less successful. When compared with final reports from responsive mode grants being assessed around the same time, the BSEP grants achieved lower grades on average, but the panel noted that this programme was tackling a relatively challenging and high-risk area of research. One of the other reasons for weak performance might be the prevalence in the programme of three-year, single-RA grants, which did not always allow sufficient time for completing research of this nature. Also, several principal investigators (PIs) had experienced technical or other difficulties and there was no clear support network for these grantholders.

Key conclusions

BBSRC should encourage PIs working in the TSE field to apply for longer, larger grants to take account of the complexity of the area and of the long time-frame required to address the key questions. If necessary there should be conditional milestones which need to be reached before further tranches of funding are awarded to the same research group.

BBSRC should consider facilitating a network for PIs in the TSE field, possibly alongside the joint funders' workshops, to enable PIs to get feedback from others and to help them to keep their research on track.

Research outputs and outcomes (pages 9-10)

The level of outputs and outcomes from BSEP was generally acceptable, although there were some exceptions. A reasonable number of refereed papers had resulted from the programme, most of which were published in well respected journals. The panel was concerned about inconsistencies in the reporting of publications by PIs in both final reports and questionnaire responses.

Other outputs reported by PIs, such as participation in TSE policy committees, follow-up funding, and new contacts and collaborations were good, but the level of public engagement activities was considered to be poor.

TSE Resource Centre (page 11)

The TSE Resource Centre, based at the Institute for Animal Health (IAH), is not meeting its objectives. A large number of resources have been deposited into the Centre by IAH researchers and are being distributed widely within the community, both nationally and internationally. However, no resources have been deposited by other research groups funded through the programme, despite this being one of the original objectives.

Key conclusion

BBSRC might usefully re-consider the requirement for the TSE Resource Centre, and should ask the Tools and Resources Strategy Panel to review its future operation, in discussion with other organisations responsible for resource centres and/or archives. It is critical to decide what materials are essential for a resource centre and what reagents should remain under the control of the investigators who generate them.

Addressing the policy needs of other funders (page 12)

Representatives from the other UK funders in the TSE field confirmed that a high proportion of the research funded within BSEP had addressed their policy needs, and that there are still several areas that would benefit from continued funding. The joint funders' workshops have been successful and provide a useful forum for discussing the progress of TSE research.

Added value

Added value was achieved from the workshops and from the creation of critical mass for UK research in TSEs. However, for further development of the area, a combination of more focused initiatives (e.g. for new investigators in the field or for the development of resources) and longer, larger responsive mode grants might be appropriate.

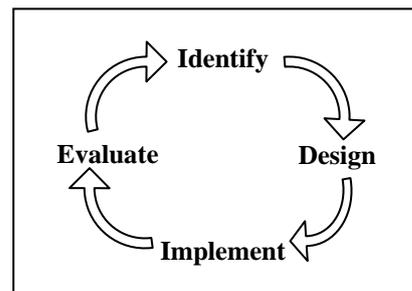
CHAPTER 1. INTRODUCTION: EVALUATION AND METHODOLOGY

Evaluation

1. The Biotechnology and Biological Sciences Research Council is one of eight Research Councils sponsored through the UK Government's Office of Science and Innovation (OSI). Its principal aim is to foster a world-class biological science community in the UK. BBSRC's mission is to fund internationally competitive research, to provide training in the biosciences, to encourage opportunities for knowledge transfer and innovation, and to engage the public and other stakeholders in dialogue on issues of scientific interest.
2. With the Government's focus on evidence-based decision making, evaluation is of growing importance to BBSRC. It informs funding decisions, it helps BBSRC to account (to Government and other stakeholders) for the funds it allocates, and it helps to improve BBSRC policy and practice.
3. **Funding decisions:** Evaluation contributes to funding decisions at a number of levels, both externally and internally:
 - Justifying funding: OSI requires research councils to bid for their future funding. Councils now have to submit evidence of the impact of the funds they allocate, to Spending Review negotiations. Evaluation provides both quantitative and qualitative evidence of achievements and impacts as part of this evidence;
 - Internal funding decisions: evaluation enables identification of achievements, progress against objectives, and reasons for lack of progress. This facilitates the development of a strategic overview, setting the framework for future funding decisions.
4. **Accountability:** as a publicly funded body, BBSRC needs to account to Government and to the general public. BBSRC also needs to be accountable to the research community it supports, and to explain its role to other relevant organisations including industry and other funding bodies. Evaluation provides evidence of achievements and progress, enabling BBSRC to demonstrate its effectiveness to stakeholders.
5. **BBSRC policy and practice:** The evidence and strategic insight discussed above is also valuable for BBSRC's policy and practice:
 - Development of policies and programmes: the results of evaluation inform policy decisions and the design of new schemes, programmes and processes;
 - Maintaining performance: evaluation enables managers to (i) share with others the lessons they have learnt and the good practice that they have developed; and (ii) identify weaknesses and improve processes.
6. Formal evaluation is conducted at a number of levels in BBSRC:

Project	<ul style="list-style-type: none">• Evaluation of final reports from grants
Scheme	<ul style="list-style-type: none">• Evaluation of research committee responsive mode portfolios• Evaluation of research initiatives (time-limited research funding in strategically significant areas), generally two to three years after the grants have ended
Institution	<ul style="list-style-type: none">• Institute Assessment Exercise, conducted every four to five years at the BBSRC-sponsored research institutes

7. BBSRC recognises that evaluation does not end with a report. Results are fed back, via Strategy Board, into policy-making, programme design and operation, as depicted by the bold arrow in the programme cycle. Evaluation thus becomes part of the evidence, experience and expert judgement used to make policy decisions and manage programmes.



Methodology

8. BBSRC has run a series of research initiatives in the Biology of the Spongiform Encephalopathies. This evaluation focuses on phases 3 and 4 of the programme; for further details of the overall programme see Appendix 2, and for grants awarded see Appendix 3.
9. This evaluation comprised two main elements: surveys of grantholders and other key players, and a review of the survey results by an expert panel.

Surveys

10. Information was gathered from a range of sources:
- **Grantholders:** 29 grants were awarded to 24 principal investigators (PIs) within phases 3 and 4 of the programme. A questionnaire was sent to each PI requesting information on a range of topics such as outputs and outcomes, networking and collaboration, further funding, and whether or not the project met its original aims. In addition, the TSE Resource Centre was asked to submit a progress report on its activities. The results of the PI surveys are presented in Appendix 4.
 - **Other relevant UK funding bodies:** representatives from other funding bodies with an interest in TSE research were invited to comment on the relationship of BBSRC's funding in this field to their organisations' interests and policy needs.
 - **BBSRC data:** relevant data were collated, including the final reports submitted by PIs, and information from BBSRC's grants databases. Review panel members each reviewed a sample of grants in advance of the panel meeting. The assessments of final reports are summarised in Chapter 2.

Review

11. The role of the review panel was to provide an independent scientific evaluation of the data presented. The panel comprised experts who are familiar with the research in this area and included two members from overseas (see Appendix 1).
12. This report will be presented to BBSRC's Strategy Board in Spring 2007. Strategy Board is responsible for analysing the report and for acting on it as appropriate. The report will also be made public on BBSRC's website, and circulated to all those who returned questionnaires.

CHAPTER 2. RESEARCH OUTPUTS AND ACHIEVEMENTS

Research quality

13. All principal investigators (PIs) funded by BBSRC are required to submit a final report within three months of the completion of their grant. The reports are assessed and graded by BBSRC Committee members (or other appropriate assessors) on a scale of A to D, taking account of the quality of the research undertaken and the extent to which it has met the initial objectives of the project¹.
14. An analysis of the final report scores awarded to grants under phases 3 and 4 of BSEP shows that half were graded A or B, indicating that these projects had added significantly to knowledge and met the majority of their objectives. The final reports for the BSEP grants were also reviewed by the BSEP review panel, who agreed in most cases with the views of the original assessors. Some grants had produced excellent results, but a number of grants had not met their original objectives and had resulted in few or no outputs.
15. When compared with the final report grades for responsive mode grants completed in 2001-02 (i.e. assessed around the same time as the phase 3 and 4 grants), the BSEP grants did not rate as highly as the responsive mode grants. There were fewer at both grade A (14% compared with 32% in responsive mode) and grade B (36% compared with 46% in responsive mode).
16. In view of the nature of TSE research, the panel identified several possible reasons for the differences between the BSEP awards and responsive mode grants:
 - Studies into TSEs tend to be experimentally complex, take a long time to complete and are often not achieved within a standard three-year grant. Some PIs had faced technical or other difficulties during the grant and did not start to produce results until the end of the grant, when the funding was due to finish.
 - Even though BBSRC encourages PIs to apply for longer-term funding, very few actually do so. This might be due to the fact that the majority of BBSRC's responsive mode grants were for three years originally so PIs tended to apply for three-year funding, rather than considering what would be the most appropriate model to enable them to meet the proposed objectives.
 - Some of the grants were for fairly high-risk research, which was not always successful. However, the panel agreed that it was important to continue to fund this type of research, and for BBSRC to provide more support for the PI throughout the grant to keep the research on track.
 - A number of grants were awarded to researchers new to the field. Even though some of these researchers had excellent track records in their own disciplines, it took them some time to establish themselves in a new field and to start producing results. Others simply proved incapable of delivering. Perhaps more attention to whether an applicant has delivered previously, even in another field, might help to avoid making such unproductive awards in future.

¹ A: Very high class work that has produced results of considerable scientific importance in a cost effective way and met all or almost all of the agreed or related key objectives

B: Work that has added significantly to knowledge in the field and met the majority of its agreed or related key objectives

C: Work that has fallen short of the contribution to knowledge or cost effectiveness expected from the original proposal even though it may have met some or all of its agreed or related key objectives

D: Work that has not added significantly to knowledge in the field and/or has failed to address the agreed or related objectives.

- With hindsight, some of the assumptions made in grant applications may have been naïve. For example, some claimed that support would be available in certain areas, or that certain reagents would be made available to them, but such support had not transpired. It is important to ascertain that an applicant does have the facilities/reagents needed, or put milestones in a grant, so that further funding is not awarded if milestones are not met.
 - There was a change in the regulations regarding animal containment during the period of the programme, which may have affected the progress of some of the grants, and was likely to have had serious practical and financial implications.
 - Some grants were awarded for testing hypotheses. In some cases the hypotheses were disproved, which affected the future direction of the research. The panel suggested that BBSRC should make it clear to PIs that there is flexibility in grants, and that they can seek BBSRC approval for changes to the objectives depending on the outcome of early experiments.
17. The panel noted that most of the more successful projects had been carried out by researchers who were members of larger teams, for example, those at the Institute for Animal Health (IAH). One of the reasons for this might have been because those researchers also receive funding from BBSRC via the institute's Core Strategic Grant, in addition to the funding via BSEP. Altogether, therefore, the IAH researchers generally made up a viable and dynamic research group. However, some of the grants held at IAH were less successful.
 18. The panel identified several grants within BSEP that were very successful, the outcomes of which were used for informing future research by BBSRC and other funders in the TSE area. One grant had provided the basis for the science underpinning the national strategy for the control of scrapie in the UK sheep population, which had major policy implications.
 19. The panel thought that BBSRC should provide more support for grantholders who were experiencing technical difficulties in their grant, or were new to the TSE field, to keep them on track throughout the progress of their grant. This might be achieved by setting up a network, perhaps alongside the joint funders' workshops (see also page 10). However, it is also important to ascertain that the institution has appropriate infrastructure/support to ensure work on any grant is properly completed. The panel noted that PIs in some EU-funded networks are required to attend regular meetings to discuss the progress of their research and this is seen as a useful mechanism to maintain contact and address emerging problems.

Research outputs and outcomes

20. A questionnaire was sent to the 24 PIs in receipt of the 29 grants in phases 3 and 4 of BSEP. The main findings are set out below; for more detailed analysis of the responses see Appendix 4.
21. The panel felt that the outputs and outcomes from BSEP were generally acceptable, even though at face value they were below the level expected from international quality research in responsive mode. Moreover, the two panel members from overseas commented that TSE research in the UK compared well with research being funded elsewhere in Europe, and that the breadth of subjects being covered by all the UK funders was impressive. US researchers had experienced very similar problems to those in the UK - including problems getting established in the field in the first place, and a lack of a critical mass of researchers to provide support during the projects.
22. On specific outputs the panel noted the following:
 - **Publications:** 91 refereed papers had resulted from the programme, most of which were published in well respected journals. The panel considered this to be a reasonable number and noted that the total is likely to be an underestimate as there was no updated information for eight (30%) of the grants for which the PIs did not return questionnaire responses. The panel expressed concern about inconsistencies in the way that PIs reported publications in final reports and questionnaire responses. Some PIs had reported publications that had been published immediately after the project had started (possibly resulting from previous phases of BSEP or from other projects), some PIs who received two grants sent one list to cover both grants and did not distinguish between them, and some had listed publications in their final reports as 'in press' or 'submitted' that were not subsequently published.

Some panel members commented that it would be helpful for future evaluations if PIs were asked to include data on the percentage contribution by individual authors on papers, and for citation figures to be provided.

- **Tools and resources:** in addition to the TSE Resource Centre (see page 11), four grantholders had developed new tools and resources. The mathematical models developed by one of the projects were considered to be a highlight of the programme, as they had provided the science underpinning the national strategy for the control of scrapie in the UK sheep population.
- **Contribution to the reduction, refinement and replacement of animals in research (3Rs):** the panel felt that this output was not especially appropriate to the research funded by BSEP, although eight PIs reported that their research had contributed to the 3Rs. These included a reduction in the number of animals used in experiments and the use of new culture systems as an alternative to using animals.
- **Participation in TSE policy committees:** the panel was impressed by the number of PIs who had been asked to join policy committees in the TSE area, with one respondent having considerable involvement in both national and international TSE committees and working groups.
- **Public engagement:** the panel was disappointed at the level of public engagement activities and agreed that it was lower than would be expected. However, the panel acknowledged that, although public engagement activities are now a requirement for BBSRC-funded PIs, this had been introduced relatively recently and may not have been in place during phases 3 and 4 of BSEP. Also, many PIs who use animals in their

research are reluctant to talk about it and some institutions have strict rules on who is allowed to speak publicly about their research.

- **Trained staff:** the panel agreed that the prevalence of three-year grants was likely to have had a detrimental effect on attracting good post-doctoral researchers as they did not provide any career stability.
- **Contacts and collaborations:** the panel was pleased to see that a number of new contacts had arisen from participation in BSEP, many of which had resulted in formal collaborations between research groups.
- **Follow-up funding:** most of the PIs who had applied for follow-up funding had been successful, with several receiving funding through the later phases of BSEP (phase 5 and a subsequent initiative in TSE diagnostics).

Workshops

23. The panel agreed that the joint funders' workshops associated with BSEP were very useful and panel members who had attended them said that they were very well run. They were particularly helpful for newcomers to the field and provided a confidential forum for discussion of research results.
24. The panel recommended that a formal session should be introduced into the workshops, where PIs funded within the programme would be required to provide an update on their project, and gain feedback from others. Although the panel recognised that it may not be feasible to run this alongside the workshops in their current format, as they cover a large number of projects, it felt that BBSRC and the other funders should consider the possibilities when planning future joint workshops.

Aims and objectives

25. The panel noted that just over two-thirds of PIs had said in their questionnaire responses that their project had met its objectives and that five of the six overall objectives of the programme had been met. The aim of ensuring full exploitation of skills and expertise was thought by PIs to have been less successful.

TSE Resource Centre

26. The panel considered the function of the TSE Resource Centre, based at the Institute for Animal Health. The Centre was established in 1998 under phase 3 of the programme, to supply a range of specialised research reagents needed for TSE research. BSEP grantholders are required to deposit reagents generated in their research in the Centre. The intention was that, by providing an infrastructure to produce sufficient amounts of quality reagents to meet the needs of users, much of the un-funded workload and cost that would otherwise be placed on individual laboratories in supplying materials would be removed, and reagents would be available for prompt distribution.
27. The Resource Centre has maintained a wide range of reagents that originated from research at IAH and has supplied these to TSE researchers worldwide. However, no reagents have been submitted to the centre by other research groups, despite the stated expectation by all the five UK funders of TSE research that reagents generated in the projects that they support should be submitted to the Resource Centre once the relevant work has been published.
28. The panel was not convinced of the added value of the Resource Centre, and agreed that, in its current form, it is not meeting its intended objectives. In particular, it has not met one of its original aims - to collect reagents from all PIs funded within the initiative. The panel agreed, however, that it is very difficult to force PIs to deposit reagents when there is no obvious incentive to do so.
29. The panel was also unconvinced by the BBSRC recommendation that the Resource Centre should start operating on a full cost recovery basis at the end of the current grant in 2008. They agreed that this would be likely to increase the costs of providing reagents and so would result in researchers contacting the scientists direct for reagents, further reducing the requirement for the Centre. The issues of quality control and IP rights would also need to be addressed if charging full costs for the provision of reagents.
30. The panel was in favour of keeping these important resources and of making them available within the community but was unsure if this should be BBSRC's responsibility. The panel noted that other centres are in place, such as the TSE tissue archive at VLA which operates on a much bigger scale and costs over £1M a year to run. The panel suggested that BBSRC should discuss this issue with other interested parties, and identified the BBSRC Tools and Resources Strategy Panel as the most appropriate body to take this forward.

CHAPTER 3. ADDRESSING THE POLICY NEEDS OF OTHER FUNDERS

31. Representatives from other UK funders of TSE research were asked to comment on the extent to which the research funded in BSEP phases 3 and 4 related to their interests or had addressed their policy needs. The comments are summarised below:
- **Department for Environment, Food and Rural Affairs (Defra):** although the political drivers concerning TSEs in livestock have reduced in intensity, approximately half of the research funded within BSEP contributed to the needs of Defra. There remains a requirement for research to meet the Departmental objectives of eradicating TSEs in cattle by 2010. The key areas include: the nature and cellular biology of the agent; TSE strain types and their importance; withdrawal of feed controls; and TSEs in sheep. Defra's policies in this area are being directed by the EU Commission through the implementation of the TSE Roadmap.
 - **Food Standards Agency (FSA):** BSEP-funded research has in part underpinned FSA's policy to protect the public via the food chain, with approximately 40% of projects working towards this aim, in particular the work on pathogenesis. However, the FSA's current emphasis is on pre-mortem testing, and they have recently awarded a small number of grants in the area, although none of these had their origins in BSEP.
 - **Medical Research Council (MRC):** research within BSEP met some of MRC's policy needs, particularly with respect to addressing questions related to the underlying biology of prion disease and neuropathogenesis. Some areas of research would benefit from further development and investment by both BBSRC and MRC, including more research into the cell biology of the disease and normal PrP function.
 - **Department of Health (DH):** research in BSEP has been critical to the Department's policy development and they have been dependent on BBSRC to fund research on animal models. The research carried out at IAH on transmission through blood has made a major contribution to the DH's risk assessment strategy, and has enabled the department to fund further important work at IAH on risks associated with blood transfusion. DH's risk assessments would be compromised in this area if it were not for this research and the development of a cadre of expertise in IAH.
32. The panel concluded that a high proportion of the research funded within BSEP phases 3 and 4 addressed the policy needs of other UK funders and that there is a requirement for continued funding by all partners. The panel considered that the funders work well together, helped by the regular dialogue between them, for example at the joint funders' workshops.

CHAPTER 4. CONCLUSIONS

33. The research funded in BSEP phases 3 and 4 provided some valuable scientific insights. A small number of projects had produced outstanding results that had underpinned subsequent research and policy development.
34. The number and quality of outputs from the BSEP grants were acceptable overall, but were not directly comparable with research outputs from responsive mode grants. The output from a few BSEP grants was unacceptable.
35. The success of the grants and the level of outputs and outcomes might have been improved by awarding more sustained funding through fewer, longer-term grants, rather than through traditional three-year, single-RA grants.
36. Some PIs had experienced technical or other difficulties during their projects. BBSRC should consider introducing a formal network, possibly alongside the joint funders' workshops, where PIs would be required to provide an update on their project, to get feedback from others and help to keep their research on track.
37. The TSE Resource Centre is not meeting its objectives and BBSRC should re-consider the requirement for it. The Tools and Resources Strategy Panel could be asked to review its future operation, in discussion with other organisations responsible for resource centres and/or archives.
38. Some of the research funded under phases 3 and 4 of BSEP addressed key policy needs of other funders at the time of the programme; there is a continued need for coordinated research in the TSE field.
39. The best of the projects in BSEP phases 3 and 4 would compete well in responsive mode, and there now appears to be little added value or obvious advantages in funding TSE research through directed programmes rather than through normal responsive mode funding. It may be more appropriate to use initiatives to stimulate grants in specific areas of TSE research, for the development of resources, or for start-up grants for PIs who are new to the field.