



## REPORT BACK FROM THE SEAC SHEEP SUBGROUP

### Issue

1. This year the SEAC sheep subgroup has considered two issues relating to the National Scrapie Plan (NSP). The group considered the implications of the first report of PrP<sup>Sc</sup> in the brains of ARR homozygote sheep for the NSP and reviewed the scientific validity of strategic options for the NSP in the light of a number of recent scientific findings. The subgroup's conclusions are presented to committee for comment and endorsement.

### Membership of Sheep Subgroup

2. The sheep sub group was previously chaired by Peter Smith, who has now retired from the Chair. Professor Higgins will now take up the chair of this group. The membership of the sheep subgroup is fluid as it will reflect issues under discussion but as a core, the group includes SEAC members and experts in sheep TSE surveillance, neuropathology, diagnostic tests, epidemiology and mathematical modelling (Annex 1).

### The NSP

3. The aim of the NSP is to increase the level of resistance to TSEs in the national sheep flock to eventually eradicate all TSEs, with the dual aim of reducing the possible risk to human health from the theoretical possibility of BSE in sheep. To this end the NSP breeding strategy is to promote the use of the ARR allele (considered the most resistant) and exclude the VRQ allele (the most susceptible), and allowing the use of sheep with the AHQ, ARH and ARQ allele for a limited period.

### POSTAL CONSULTATION

4. The sheep subgroup was consulted in March 2004 following reports that PrP<sup>Sc</sup> had been detected in the brains of ARR/ARR sheep. This genotype was previously thought to be naturally resistant to scrapie.

5. The sheep subgroup was asked to consider if the new scientific development had any implications for the scientific basis of the NSP. In summary, the sheep subgroup "*endorsed their previous opinion of 11 December 2002 that the strategy to increase resistant genotypes and decrease susceptible genotypes was scientifically justified. Although the current evidence suggests that the ARR/ARR genotype is not completely protective against natural TSE infection, the relative protection, compared to other genotypes, remains very large*". The summary of the subgroup's responses is attached at Annex 2.

#### **Question for the committee**

6. Does the committee have any comments on the conclusions of the sheep sub-group postal consultation?

### **CONSULTATION ON OPTIONS FOR THE NATIONAL SCRAPIE PLAN**

#### **Issue**

7. Defra is consulting stakeholders regarding future strategic options for the NSP. As part of this process, the SEAC sheep subgroup met on 26<sup>th</sup> July 2004 to consider four future options for the NSP and their scientific validity in the light of emerging scientific research findings.

#### **Question for the committee**

8. SEAC is asked to note and comment on the conclusions of the sheep subgroup regarding the options presented for the NSP.

#### **Background**

9. Over the last year Defra developed a number of strategic options for a suitable vehicle to meet its obligation to introduce a compulsory genotype based breeding programme in April 2005 as required by European Commission Decision 2003/100/EC. These options were modelled by Simon Gubbins, VLA (now at the IAH) and Janet Roden, Institute for Rural Science, University of Wales, Aberystwyth. Each option was modelled to assess the resulting changes in the genotype profile of the national flock and the impact on the prevalence of scrapie infection.
10. From the outcomes of this modelling work, four options were submitted for public consultation on the 21<sup>st</sup> July 2004 (Annex 3).

The consultation document is displayed on the Defra website at: <http://www.defra.gov.uk/corporate/consult/nsp-stratreview/consultation.pdf> Copies of the consultation document and report on the modelling of the options can be obtained from the SEAC secretariat.

11. In recent years there have also been a number of scientific developments that could have impacted on the future operation of the NSP on which SEAC's views have been sought (see Annex 4).

### **Questions to the SEAC sheep subgroup:**

12. Defra asked the SEAC sheep subgroup if in light of current scientific developments:

- (i) Does it remain the opinion of the subgroup that breeding for increased resistance to scrapie in the national flock is still appropriate?
- (ii) Their opinion on the advantages and disadvantages associated with each option.

13. The sheep subgroup agreed the statement below but asked that further modelling work be undertaken to consider mandatory Option B combined with voluntary Option D. The modelling has been completed and circulated to the sheep subgroup for comment. SEAC will be updated on the outcome at the meeting on 28 September 2004 or in writing.

### **Statement from the sheep subgroup**

*“Defra is consulting stakeholders on four strategic options for the future operation of the National Scrapie Plan (NSP). The SEAC sheep subgroup's views were sought as part of this consultation.*

*The subgroup concluded that the strategy of the NSP underlying breeding for scrapie resistance remains appropriate. However, the basis for the strategy should be kept under review in the light of emerging scientific findings with respect to the possible detection of scrapie infections in animals of genotypes currently thought to be most resistant to infection.*

*The subgroup was of the view that those strategies that reduced the prevalence of infection in the national flock most rapidly were the most desirable. On this basis Option A was considered*

*inadequate. The subgroup considered that although Options A and B addressed scrapie in VRQ sheep these would not reduce scrapie in ARQ sheep or the hypothetical possibility of BSE in sheep, which targets the ARQ allele. The subgroup considered a solution closer to Option D was the most scientifically desirable given the importance of reducing the prevalence of scrapie and the potential risk of BSE. However the subgroup recognised that there were practical difficulties and in some cases genetic constraints for the sheep industry and cost issues, which were issues for Government that would need to be taken into account in determining the chosen option.”*

**MEMBERSHIP OF THE SEAC SHEEP SUBGROUP (JULY 2004)**

<b>Members</b>	<b>Affiliation</b>
Professor Peter Smith (Chair)	SEAC
Professor Chris Bostock	SEAC
Professor Robin Carrell	SEAC
Mr Peter Jinman	SEAC
Professor Ian McConnell	SEAC
Dr Jean Manson	SEAC
Dr Wilfred Goldman	IAH Edinburgh
Dr Nora Hunter	IAH Edinburgh
Professor Neil Ferguson	Department of Infectious Disease Epidemiology Imperial College, London
Dr Fiona Houston	IAH Compton
<b>Advisers</b>	
Professor John Wilesmith	Defra
Dr Danny Matthews	VLA
Dr Jim Hope	VLA
Dr Janet Roden	University of Wales, Aberystwyth
Dr Simon Gubbins	Formerly VLA, now IAH Compton
Mr Mike Dawson	NSPAC
Dr Marion Simmons	VLA

IAH            Institute for Animal Health  
VLA            Veterinary Laboratories Agency  
NSPAC        National Scrapie Plan Admin Centre  
SEAC         Spongiform Encephalopathy Advisory Committee

**SEAC sheep subgroup postal consultation March 2004  
Summary of responses**

1. In 2003 two cases of natural TSE infection were reported by the German authorities in sheep of ARR/ARR genotype, previously associated with resistance to scrapie. Both of these animals were aged 2 years. One was found dead on farm and the other was identified through the TSE testing of healthy animals at slaughter. Neither case was recognised through the identification of clinical symptoms of scrapie. In the light of these cases and the publication of the European Food Safety Authority (EFSA) opinion on TSEs in sheep in November 2003, the SEAC sheep subgroup was asked to consider if the finding of natural TSE infection in ARR/ARR sheep in the German cases has any implications for the scientific basis of the National Scrapie Plan (NSP).
2. The subgroup noted the importance of the finding of natural TSE infection in ARR/ARR sheep as it shows this genotype can acquire infection by natural routes as well as experimentally by intracerebral inoculation. The issues of the possible carrier status of ARR/ARR sheep, with respect to TSE infections, and whether there are rare TSE strains that preferentially target ARR/ARR sheep, remain of concern. However, the subgroup endorsed their previous opinion of 11 December 2002 that the strategy to increase resistant genotypes and decrease susceptible genotypes was scientifically justified. Although the current evidence suggests that the ARR/ARR genotype is not completely protected against natural TSE infection, the relative protection, compared to other genotypes, remains very large.
3. The subgroup reiterated the importance of maintaining a bank of genotypes removed from the national flock. This would be important if it is found that removal of susceptible genotypes takes out other phenotypically valuable attributes from the UK flock or if new findings emerge that indicate that the ARR/ARR genotype has less resistance to natural TSE infection than currently appears to be the case.
4. The subgroup stressed the importance of active surveillance to determine the prevalence of TSE infections in the sheep population and to acquire additional data on the relationship between genotype and natural TSE infections. The subgroup concurred with the November 2003 EFSA opinion that currently used BSE rapid tests should be validated for TSEs in sheep, taking into account the possible influence of genotype on the performance of the tests.

## Options for the National Scrapie Plan

### **Option A EU minimum**

The EU minimum rules require the genotype testing of all rams intended for breeding within flocks of 'high genetic merit' (Defra are proposing to apply the definition of 'high genetic merit' to all pure-bred flocks which sell homebred rams for further breeding) and the subsequent slaughter of those found to be carrying the VRQ allele (compensation will be paid for animals slaughtered). It does not require the genotype testing of rams sold for breeding elsewhere. Consequently, the sale of untested (and hence possibly VRQ) rams for further breeding is not prohibited. However, any untested rams purchased for use within another flock of 'high genetic merit' would need to be genotyped before being used for breeding and those carrying the VRQ allele removed in line with the requirements of the EU legislation.

### **Option B**

**EU minimum plus additional genotyping of rams\shearlings\ram lambs intended for sale and further breeding elsewhere.**

In addition to the EU minimum requirements as described above at Option A, this option would also provide for the genotype testing in all flocks of 'high genetic merit' of rams\shearlings\ram lambs intended for sale and further breeding irrespective of whether they are to be used in other flocks of 'high genetic merit' or elsewhere further down the breeding pyramid e.g. in a commercial fat\slaughter lamb producing flock.

### **Option C**

**EU Minimum plus additional ram testing as Option B and voluntary ewe testing during the period 2005-2010 conditional on the removal of ARQ/ARQ breeding rams in participating flocks from 2010.**

As Option B above, with an additional voluntary ewe genotyping scheme\service targeting female replacements conditional on the removal of ARQ/ARQ breeding rams from participating flocks from 2010. The Option is currently based on testing 200,000 female replacements across all sheep sectors per year. This is an indicative

figure based on possible field and laboratory testing resource considerations (and may require fine tuning).

**Option D**  
**Compulsory NSP Ram Genotyping Scheme (RGS)**

The current voluntary NSP's RGS provides for the genotyping of all existing stock rams and for the removal of those carrying the VRQ allele. It also applies sale and on farm use restrictions for Type 3 (ARQVAHQVARH) rams (end 2005 and 2008 respectively for terminal sire breeds and end 2007 and 2009 respectively for hill breeds). Additionally, it also provides for annual progeny testing of males (and females where there are fewer than 40 male animals available for testing i.e. each testing visit will comprise 40 animals in total) intended for further breeding. Under Option D, these arrangements would be made compulsory for all flocks of 'high genetic merit'.

### Scientific developments

1. The report from the Institute for Animal Health (IAH) that scrapie free ARR/ARR New Zealand sheep intracerebrally challenged with BSE developed clinical disease (Houston et al, 2003<sup>1</sup>). SEAC were asked in December 2002 for their opinion on this result and what the scientific implications for the NSP were. SEAC concluded that *“although this research shows that ARR/ARR may not be fully resistant to infection, increasing resistant alleles in the national flock would reduce the potential sources of infection and thus reduce the incidence of clinical disease. This would have the ultimate effect of reducing the possibility of potential human exposure to BSE infectivity via the food chain. [SEAC] Members agreed this latest research is a significant development but they did not consider that the new research undermined the scientific basis of the NSP”* .
2. Samples from the abattoir survey that were positive by Bio-Rad ELISA but could not be confirmed by either Western blot or immunohistochemistry (IHC). These findings were reported in September 2003 to a special expert group who *“recognised the importance of these findings but agreed that, due to the lack of data, it was not possible, at this early stage, to draw any firm conclusions about the basis for and significance of the discrepancies reported.”* In November 2003 the expert group’s opinion was reported to SEAC, which concurred with their conclusions.
3. Reports from France and Germany where they have detected PrP<sup>Sc</sup> in the brains of ARR/ARR sheep. Following a postal consultation in March 2004 the sheep subgroup *“endorsed their previous opinion of 11 December 2002 that the strategy to increase resistant genotypes and decrease susceptible genotypes was scientifically justified. Although the current evidence suggests that the ARR/ARR genotype is not completely protective against natural TSE infection, the relative protection, compared to other genotypes, remains very large”*. (This opinion is being presented to the main SEAC committee for its comment and approval see section A above.)

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<sup>1</sup> Houston, F., Goldmann, W., Chong, A., Jeffrey, M., Gonzalez, L., Foster, J., Parnham, D. and Hunter, N. (2003). BSE in sheep bred for resistance to infection. *Nature* **423**, 498

4. The recent report from the Veterinary Laboratories Agency (VLA) of a sample that appeared to have some similarities with experimental BSE in sheep using Western blot, however IHC appeared to indicate that the sample did not resemble BSE or any scrapie strains previously investigated by the method. At a meeting of scientists with expertise in differential diagnostic tests it was concluded that this case could not be considered to be BSE in sheep, although it does not behave like known types of scrapie either. When this finding was presented to SEAC in April 2004 they were content with this conclusion.

