Extract from the minutes of the meeting of 14-15 September 2000 on some TSE-issues that recently emerged in the scientific and popular press

At its meeting of 14-15 September 2000, the SSC also discussed the following issues as a follow-up to the TSE/BSE *ad hoc* Group meeting of 31 August 2000.

1. A recent brief Communication in Nature (10 August 2000), suggests that, on average, no more than two cases of vCJD could arise from the consumption of one maximally infected bovine, as opposed to previous estimates that this number could exceed 100. This would result in a significant reduction of the expected maximum number of future vCJD cases.

The SSC noted that this short Communication contains quite limited scientific details and that the model leading to the results on which the conclusions are based, contains many assumptions. It noted that in an earlier publication of January 2000, the same research team accepted a **much wider** range of up to more than 100 vCJD cases that could arise from 1 maximally infected bovine. **The assumption is made that only those with the presently observed susceptible genotype are at risk. Also**, the communication does not take into account the most recent raise in numbers of vCJD cases. The SSC considers that in the field of TSEs there are still so many unknowns that it is very difficult to make predictions on future numbers possibly to be expected, especially in this stage of the epidemic.

2. Prof.S.Prusiner's recent hypothesis (reported on in the Sunday Times of 23 July 2000) that BSE prions in sheep may have been there all the time at very low levels that pose no significant risk to humans but that unusual circumstances might have allowed them to spread either through the sheep or cattle population and accumulate to levels hazardous to humans.

The SSC noted the outcome of the e-consultation of Europe's main TSE experts organised by its secretariat in July 2000, which was in line with the final clarification provided on 2 August 2000 in a letter from Prof.Prusiner to the SSC Secretariat. BSE was not produce in mice by infecting them with material suffering from scrapie but both sheep scrapie and BSE prions had been transmitted to mice which are engineered to mimic cattle. From his findings Prusiner *et al* advance the *hypothetical* scenario that "it is possible that low levels of the BSE 'prion strain' are actually endemic in the scrapie sheep population, but that the BSE prions never surface as such because their presence is marked by the more rapidly growing sheep scrapie strain. Any unusual selective treatment, such as the change in rendering process, could remove the less dangerous sheep scrapie strain and allow the BSE strain to accumulate and spread to the cattle population". In conclusion, "BSE prions in sheep may thus have been there all the time at very low levels that pose no significant risk to humans but unusual circumstances might have allowed them to spread either through the sheep or cattle population and accumulate to levels hazardous to humans."

The SSC considered, as for the Collinge paper (see hereafter), that the Prusiner hypothesis in its present form (i.e., without published details) does presently not trigger the need for an immediate revision of the SSC's various "TSE in sheep" related opinions. It is, however, obvious that Prof.Prusiner's research and similar work by others, will be monitored carefully and, once finalised and published, further assessed by the Working Group presently carrying

out a pro-active risk assessment for the case that BSE in sheep would be found under natural conditions.

3. The Hill *et al* publication (" *the Collinge paper*") in the Proceedings of the National Academy of Sciences (August 2000) on the possible presence of subclinical TSE infectivity in certain animals and its implications for the definition of cross-species barriers of TSE transmission.

The SSC considers that most of the scientific evidence on which the paper is based, was either known to it or anticipated by the SSC and has been appropriately addressed in various scientific opinions. As a matter of principle, the SSC has not based its risk assessments with regard to the safety of animals on results of end-point titrations with clinical disease in laboratory animals as the sole parameters. Furthermore, the SSC reviews and updates its existing opinions in the light of emerging scientific data, on regular basis. The relevance of 4 of the SSC opinions with regard to the Collinge-paper, is summarised in annex. The following incomplete list of SSC recommendations, can be presented as an example on how the possible existence of subclinical infections with important public health implications with relation to dietary exposure, have already been taken into account in the SSC opinions:

- **Product safety** (gelatine, tallow, meat-and-bone meal, dicalcium phosphate, ...): the opinions start from the hypothesis that an animal with TSE, but apparently healthy, would be slaughtered and assume *a very low species barrier*. The recommended production standards aim, when a TSE risk cannot be excluded, for safe sourcing of raw material, removal of SRMs and severe processing conditions.

- **Geographical risk**: a risk level is attributed to the ruminants of countries or regions where BSE might be present, even if no clinical case have been detected.

- **SRMs**: removal of the ruminant tissues with the expected highest infectivity levels, should they be slaughtered without a TSE having been diagnosed;

- No further use of **fallen stock** and certain animal categories, as a TSE could be at the basis of the death or could be [undiscovered] present in certain animals.

- Avoidance of **intra-species recycling** (see annex for details).

The SSC concluded that there is at present no need to revise its TSE-related opinions. It, however, asks its secretariat to request from the UK and the EC research authorities the most up-to-date research results on TSEs in pigs, poultry and in fish. From an analysis of this info should appear whether there is a need to revisit certain opinions.

It also asks the TSE/BSE *ad hoc* Group to assess whether there is a need for an adaptation of TSE surveillance strategies in farmed animals and whether there is a need to update the opinion on breeding for scrapie resistant sheep as a means to control TSEs in small ruminants.

***Annex*: The relevance of 4 SSC opinions with regard to the Collinge paper (August 2000).**

The TSE/BSE *ad hoc* Group considers that most of the scientific evidence on which the paper is based, was either known to or anticipated by it and has been addressed in various scientific opinions. To be mentioned especially are:

a. The Opinion of 24-25 June 1999 on The risks of non conventional transmissible agents, conventional infectious agents or other hazards such as toxic substances entering the human food or animal feed chains via raw material from fallen stock and dead animals (including also: ruminants, pigs, poultry, fish, wild/exotic/zoo animals, fur animals, cats, laboratory animals and fish) or via condemned materials.

b. The opinion of 22-23 July 1999on the policy of breeding and genotyping of sheep, i.e. The issue of whether sheep should be bred to be resistant to scrapie.

c. The opinion of 17 September 1999 on the risk born by recycling animal by-products as feed with regard to propagating TSE in non-ruminant farmed animals.

d. The opinion of 13-14 April 2000 on Oral exposure of humans to the BSE agent: infective dose and species barrier. (Adopted following a public consultation via internet between 6 and 27 march 2000)

The **first opinion** considers the risk to the public, to animals and to the environment from transmissible biological and chemical agents which may be present in fallen stock and dead animals. The opinion makes recommendations on how such risks can be minimised. In the light of experience with BSE this includes consideration of unconventional and as yet unknown agents. The risk to man from dead animals and condemned materials is considered to depend on:

- The nature and level of the agent(s) present in the dead animal / fallen stock, which in turn relies on accurate diagnosis and measurement;

- The prospect of intra and interspecies transmission;

- The actual processing / disposal method used;

- The prospects of human exposure as a consequence of the processing / disposal.

Whilst also addressing zoo-, laboratory-, exotic- and pet animals, the opinion states, with respect to the susceptibility of pigs, poultry and fish to become infected with TSEs is concerned, that there is only evidence that pigs can become infected through intra-cerebral inoculation with infectious BSE material. To date no experiments have shown that pigs, poultry or fish could be infected with TSE *via* the oral route. Whilst recognising that experimental transmission *via* the i/c route has been shown for a number of animal species, the to date not proven hypothesis that orally TSE-inoculated non-ruminants without any signs of disease could carry the TSE-infection in their tissues has is considered unlikely.

The **second opinion** addresses, amongst other issue, that an animal not showing clinical signs can be infectious. It mentions the experimental evidence for the existence of hidden infectivity. It clarifies that "resistant" sheep may include animals that remain clinically free of

scrapie *signs* for normal life-span but could still harbour the infectious agent, posing a threat by maintaining the infectious agent. It points at the possible existence, for sheep, of carrier animals with latent scrapie infection, that will not itself develop disease but with the ability to pass infection on to other sheep. This opinion also states that cross species persistence may also occur: hamster scrapie injected into mice does not produce disease but the hamster scrapie remains in brain and spleen of the mice and can be recovered in a form still able to infect hamsters. The SSC concludes, amongst others, that the possibility that sheep may harbour a latent scrapie infection exists and if so, that they could pass an infection to other sheep.

The **third opinion**, on intra-species recycling, stated in mid 1999, that:

"a. So far no scientific evidence exists to demonstrate the natural occurrence of TSE in farmed pigs, poultry and fish, which may create a basis for an intra-species progression of a TSE infection due to intra-species recycling.

b. Given the limitations of the surveillance in certain areas, and the length of the incubation time in relation to the normal (=economic or commercial) life span of the animals, it can not be excluded that cases occur and that, perhaps more important, an undetected pool of infectivity is build up.

c. Because of these two preceding points, the SSC wants to underline that in scientific terms absence of evidence is neitherevidence of absence nor of presence of a risk. However, it is impossible to exclude, on the basis of the available evidence, that TSEs are already present (albeit undetected) in non-ruminant farmed animals, in particular not if there is reason to assume that these species have been (and might still be) exposed to BSE-contaminated feed (produced from ruminants).

d. Recycling of animal material, in general, will increase the risk that cases occur or undetected infectivity pools develop,in particular if potentially BSE (TSE) contaminated material is recycled to ruminants or (possibly) susceptible non-ruminants.

e. Intra-species recycling will, due to the absence of a species barrier, increase the risk further.

f. If recycling, and in particular intra-species recycling, of animal material to farmed animals can not be avoided, all measures that reduce the recycled infectivity would reduce the risk.

g. Measures that reduce the recycled infectivity include:

- exposing the recycled animal material to a treatment by 133°/20'/3b or equivalent conditions,

- excluding those tissues known to carry the highest infectious load (SRM),

- excluding fallen stock from the production of feed,

- stop feeding pig, poultry or fish potentially contaminated feed a sufficiently long period of time before slaughter in order to reduce the risk of recycling infectivity via the gut-content.

h. It has to be understood that

- the possible measures would not be able to reach a zero risk should infectivity enter the recycling loop, and

- that due to the long incubation time of this type of disease a significant risk would have build up before an incidence becomes visible (as has been seen in the case of BSE in the UK).

i. The SSC considers R&D in the field of surveillance and (pre-clinical) diagnostic of TSEs and the experimental transmission of TSEs to farmed (non-ruminant) animals to be of highest priority."

The **fourth opinion** states, on species barrier: "The size of the species barrier for BSE-in-ruminants to BSE-in-humans is not known and may be large (for example a barrier of the order of 1000, as assumed in some risk assessments) or small. Given the conflicting scientific data and thus the uncertainties about the bovine-to-human species barrier as outlined in this document, the assumption of a worst case scenario considering no (=1) barrier should be included, although available evidence indicates that values greater than 1 are likely to be more realistic. The Working Group therefore recommends that, until more scientific data are available, for risk assessments of human exposure to potentially BSE contaminated products, a species barrier of about 1 should considered as a worst case scenario and that, in risk assessments, the range from 10^{4} to 10^{1} is considered. The latter order of magnitude would imply that the minimal infective dose value(s) considered/accepted to be valid for animals, should also be applied for humans."