Tests for BSE evaluated

Sir — Four rapid tests for the diagnosis of bovine spongiform encephalopathy (BSE) in bovines have been evaluated by us for the European Commission[1]. Full details of this evaluation can be found in ref. 2.

We summarize here our findings on the sensitivity, specificity and detection limits of each test. Of ten tests submitted, four were accepted for evaluation on grounds such as their ability to be scaled up quickly for rapid evaluation on the timescale required. The tests were:

- **Test A (E. G. & G. Wallac):** a two-site non-competitive immunometric procedure using two different monoclonal antibodies. DELFIA technology is used to generate the reading signal.
- **Test B (Prionics):** an immunoblotting test based on a western blotting procedure for the detection of the protease-resistant fragment PrP^{Sc} using a monoclonal antibody.
- **Test C (Enfer):** a chemiluminescent ELISA, using a polyclonal anti-PrP antibody for detection.
- **Test D (CEA):** a sandwich immunoassay for PrP^{Sc} carried out following denaturation and concentration steps. Two monoclonal antibodies are used.

Tests A and D take less than 24 hours to perform, whereas tests B and C take 8 and 4 hours, respectively, and also have the highest throughput.

We evaluated sensitivity and specificity in relation to samples from true positive and true negative animals. We obtained positive samples from cows showing clinical signs of BSE and in which the disease was confirmed by histopathological examination. Negative samples were obtained from healthy cows of similar age slaughtered in New Zealand. The tissues used in the evaluation were from the same animals but were those tissues for which each test was developed: brain stem for three tests and anterior cervical spinal cord for the fourth, with a total of 1,000 negative and 300 positive samples for each test. Samples that weighed approximately 1g each were prepared, taking precautions to avoid any cross-contamination. In addition, positive brain homogenate of known infectivity titre was tested at dilutions in negative brain of up to 10^{-5} to estimate the detection limits of the tests.

Table 1 **Sensitivity and specificity using predetermined cut-off points**

	Test A	*Test B*	*Test C*	*Test D*
Sensitivity	70%	100%	100%	100%
Specificity	90%	100%	100%	100%

We carried out the evaluation under supervision at the participants' laboratories over a one-month period. Testing was done with all involved blinded, including the supervisor being unaware of the identity of the samples. We interpreted the results using a cut-off point proposed by the participants. Inconclusive categories were established in advance and it was decided that, in the case of a retest of these samples, the second result would be the valid result. Results are summarized in Tables 1 and 2.

The results indicate that tests B, C and D have excellent potential for detecting or confirming clinical BSE for diagnostic purposes or for screening dead or slaughtered animals for such cases, particularly casualty animals or carcasses sent for rendering. Even though BSE is a rare disease, the high specificity indicates that these tests may be useful for general post-mortem screening of older bovines.

Table 2 **Number of homogenate samples scoring positive (above cut-off) at each dilution level**

Dilution	*Test A*	*Test B*	*Test C*	*Test D*
0	6/6	6/6	6/6	6/6
10^{-1}	0/20	15/20 (+2?*)	20/20	20/20
$10^{-1.5}$		0/20	20/20	20/20
$10^{-2.0}$			0/20	20/20
$10^{-2.5}$				18/20
$10^{-3.0}$				1/20
$10^{-3.5}$				0/20

* Two samples rated inconclusive at this dilution.

The ability of tests to detect small concentrations of PrP^{Sc} gives grounds for optimism that they could detect infected animals before the development of clinical signs. However, the absence of information on the progression of the disease in bovines, particularly the relationship between infectivity titres and PrP^{Sc} concentration throughout the incubation period, means that it is not possible to reach any definite conclusions at this stage.

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2. European Commission *The Evaluation of Tests for the Diagnosis of Transmissible Spongiform Encepalopathies in Bovines* http://europa.eu.int/ comm/dg24/health/ & http://www.irmm.jrc.be

The land of rising science

Sir — Japan now has a greater scientific output than the United Kingdom, judging by the 1997 Japanese white paper (consultation document) on science and technology[1]. The figures for 1995 clearly show that Japan ranks second only to the United States[2] in terms of scientific output. In my opinion, the Japanese scientific contribution is underestimated in the West.

Compared with the United Kingdom, Japan has a larger population (by a factor of 2.1), a larger economy (by a factor of 4.4), spends more on scientific research (by a factor of 3.5), has a larger base of researchers (by a factor of 3.7), and awards more advanced science degrees (by a factor of 1.9)(see Table 1 in Supplementary information and ref. 3).

Japanese industry spends relatively more on research and development, whereas Japanese government institutions and universities receive less funding, than their UK counterparts. Although Japan is officially in recession, these differences are so large that Japan continues to be ahead of the United Kingdom in these categories. Science funding in Japan has continued to increase despite economic difficulties.

Japan has a 23.9% share of world exports of high-tech products, compared with the 8.3% UK share. It has a trade balance (exports/imports) of 3.52 for high-tech products compared with 0.93 for the United Kingdom.

These figures show unequivocally that Japan has a much bigger scientific base than the United Kingdom and that Japanese companies are much more engaged in research than their UK counterparts. These factors would, in part, explain Japan's dominance in technology-based industries.

In 1994, Japan produced 9.6% of the world's scientific papers published in major journals and had an 8.0% share of the number of citations of papers (see Tables 2 and 3 in Supplementary information). Corresponding figures for the United Kingdom were 9.1% and 11.6%, respectively. This undoubtedly results from the much greater increase in research and development expenditure in Japan (237%) than in the United Kingdom (126%) during 1980–95.

A fuller version of this Correspondence is at **http://www.gsj.go.jp/~kiyo/glasby.html**

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2. May, R. M. *Science* **275,** 793–796 (1997).
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Supplementary information is available on *Nature*'s World-Wide Web site (http://www.nature.com).