Advisory Committee on Dangerous Pathogens
Spongiform Encephalopathy Advisory Committee

Transmissible Spongiform Encephalopathy Agents: Safe Working and the Prevention of Infection

published by The Stationery Office
Price 10

Contents

Statement by the Health and Safety Commission about this guidance

This guidance is prepared in consultation with HSE, by the Advisory Committee on Dangerous Pathogens (which was appointed by the Health and Safety Commission as part of its formal advisory structure and by Health Ministers) and by the Spongiform Encephalopathy Advisory Committee (which was appointed by Health and Agriculture Ministers). The guidance represents what is considered to be good practice by members of the Committees. It has been agreed by the Commission and by Health Ministers. Following the guidance is not compulsory and you are free to take other action but if you do follow it you will normally be doing enough to comply with the law. Health and safety inspectors seek to secure compliance with the law and may refer to this guidance as illustrating good practice.

Advisory Committee on Dangerous Pathogens Spongiform Encephalopathy Advisory Committee

Transmissible spongiform encephalopathy agents: safe working and the prevention of infection.

This guidance gives advice on work with transmissible spongiform encephalopathy agents (TSEs) in experimental and clinical settings.

It does not cover incidental exposure such as in farms, abattoirs or other work with animals. Separate information is available and is listed in the bibliography to this guidance.

Index to tables

Abbreviations

ACDP:	Advisory Committee on Dangerous Pathogens
ACGM:	Advisory Committee on Genetic Modification
BDA:	British Dental Association
BSE:	bovine spongiform encephalopathy
CJD:	Creutzfeldt Jakob disease
CNS:	central nervous system
COSHH:	Control of Substances Hazardous to Health Regulations 1994
CSF:	cerebrospinal fluid
CWD:	chronic wasting disease
DH:	Department of Health
ENT:	ear, nose and throat
FFI:	fatal familial insomnia
FSE:	feline spongiform encephalopathy
GSS:	Gerstmann Strussler Scheinker disease
hGH:	human growth hormone
hPG:	human pituitary gonadotrophin
HSAC:	Health Services Advisory Committee
HSE:	Health and Safety Executive
MAFF:	Ministry of Agriculture Fisheries and Food
MBM:	meat and bone meal
MHSWR:	Management of Health and Safety at Work Regulations 1992
nvCJD:	distinct variant of Creutzfeldt-Jakob disease first reported in March 1996
ppm:	parts per million
PrP:	prion protein
RIDDOR:	Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995
RPE:	respiratory protective equipment
SBO:	specified bovine offal
SEAC:	Spongiform Encephalopathy Advisory Committee
SSD:	sterile services department
TME:	transmissible mink encephalopathy
TSE:	transmissible spongiform encephalopathy
UV:	ultraviolet radiation

Foreword

The announcement, in March 1996, of 10 cases of a distinct variant form of Creutzfeldt-Jakob disease (nvCJD) in young patients renewed concerns about the possibility that the bovine spongiform encephalopathy (BSE) agent could cause human disease. Research findings which have emerged since have added strong support to this hypothesis and, although many unanswered questions remain, the Governments independent Spongiform Encephalopathy Advisory Committee (SEAC) have concluded that the transmissible agent of BSE is the same as that which causes nvCJD. The Advisory Committee on Dangerous Pathogens (ACDP) embraced this conclusion, and have recommended that BSE is defined as a biological agent within the context of the Control of Substances Hazardous to Health Regulations (COSHH).

The emergence of nvCJD, and its link to BSE, emphasised the requirement to update the previous guidance for those who work with the agent and those who may come into contact with it. Consequently, the ACDP were tasked with reviewing and revising previous occupational guidance on transmissible spongiform encephalopathies (TSEs). A priority was to review the advice to those in industrial workplaces where there is contact with material that may contain, or be contaminated with, the BSE agent, for example, those involved in animal slaughter or carcase-dressing. In June 1996, the ACDP published general occupational guidance intended to help those responsible for health and safety in developing local codes of practice for safe working.

In the light of the emerging information about TSEs, it was considered appropriate also to review and update earlier advice about laboratory work, clinical care and animal handling. The present guidance is the result of this review. It updates the 1994 ACDP publication entitled Precautions for work with human and animal transmissible spongiform encephalopathies and replaces previous guidance from the Department of Health on the management of patients with CJD. It is aimed at those working with animal or human TSEs in the laboratory, and provides advice also to those involved in the management and care of patients; on the handling of deceased patients; and on the minimisation of risks to other patients and staff. Inevitably, in a rapidly evolving field such as this, there will be a need to review this guidance regularly as further information becomes available.

Although the scientific community has provided considerable insights into the nature of TSEs, there are many remaining uncertainties, for example about the routes of infection, infectious dose, and the potential number of people who may be incubating nvCJD. An important factor is that nvCJD is quite distinct from classical CJD. As well as differences in clinical presentation and pathology, particularly the microscopic appearance of lesions in the brain, early indications are that the pathogenesis of the new disease may be significantly different. For example, there may be more involvement of tissues outside the central nervous system with the possibility of infectivity in other tissues or body fluids. The full implications of the differences between the different forms of CJD will need to be assessed as more information becomes available.

The assessment of risks from TSEs embraced in this document reflects these uncertainties. Research is continuing, both under a Government sponsored programme and internationally, that is aimed at improving our understanding of these unusual diseases and the agents which cause them. The results from these studies will be incorporated in future assessments of the risks.

It is important that those concerned with, or responsible for, the well-being of workers who may be at risk of exposure to TSE infectivity (and especially their employers) should ensure that they keep abreast of further scientific developments and reflect them in working practices.

Readers are reminded that this is a guide, and new findings not covered by the guidance should always be taken into account in conducting risk assessments.

This guidance has been prepared by a joint working group of the ACDP and SEAC and has been endorsed by both Committees.

The Secretariat thanks the members of the joint working group, ACDP and SEAC for their expert advice, and all others involved, including the Microbiology Advisory Committee of the Medical Devices Agency who advised particularly on decontamination issues.

March 1998

Part 1
Background and Introduction

1.1 Transmissible spongiform encephalopathies (TSEs), sometimes known as prion diseases, are fatal degenerative brain diseases which occur in humans and certain other animal species. A common feature of all TSEs is the appearance of microscopic vacuoles (holes) in the grey matter of the brain, giving a sponge-like appearance, from which the conditions derive their name. All the diseases are experimentally transmissible by inoculation and in some cases by oral challenge.

1.2 There are several recognised TSEs, including Creutzfeldt Jakob Disease (CJD) in humans, bovine spongiform encephalopathy (BSE) in cattle and scrapie in sheep. Other related conditions are summarised in Box 1.

1.3 TSEs are in many ways unique, and exhibit biological properties that are different from those of other microbiological diseases. A useful summary about these diseases has been published previously by the Spongiform Encephalopathy Advisory Committee (SEAC) (see bibliography). Some of the important features relevant to occupational exposure are summarised below:

- TSEs are caused by unconventional infectious agents currently thought to be infectious proteins (possibly without nucleic acid) known as prions which do not share the normal properties of viruses or bacteria;

- some forms of human TSEs appear to have a solely genetic origin, whereas in other human TSEs, and in animal TSEs, there is a complex relationship between the infectious agent, host genetic factors and cellular proteins;

- TSE agents are not uniformly distributed in the tissues of affected individuals and infectivity levels vary at different stages of incubation. In general, and late in an infection, neural tissues pose the highest risk, spinal fluid and lymphoreticular tissue a lower risk and blood, other body fluids and most other tissues negligible risk;

- TSE agents exhibit an unusual resistance to conventional chemical and physical decontamination methods. They are not significantly affected by disinfectants like formalin and ethylene oxide, and infectivity persists after autoclaving at conventional times and temperatures (e.g. 121°C for 15 minutes). They are also extremely resistant to high doses of ionising and UV irradiation and some residual activity has been shown to survive for long periods in the environment;

- all TSEs are invariably fatal once clinical signs appear; there is no known treatment or prophylaxis;

- TSEs are not highly contagious and, other than sheep with scrapie, do not seem to spread from an infected host to an uninfected one by normal contact. There are documented cases of CJD being transmitted accidentally to patients via contaminated medical instruments or contaminated pituitary hormones prepared from human cadavers (these are known as iatrogenic infections);

- there have been no confirmed cases of transmission of TSE to humans as a result of occupation. If TSEs could be transmitted in the occupational setting this would be most likely to occur from exposure to infected tissues or materials by direct inoculation (e.g. puncture wounds, sharps injuries or contamination of broken skin), by splashing of the mucous membranes or, exceptionally, by swallowing.

1.4 The unconventional nature of the agent, together with the appearance of BSE in the mid 1980s and a new distinct variant CJD (nvCJD) in the mid 1990s, has led to a considerable amount of scientific research. This in turn means that there is a need for updated guidance on safe work practices in laboratories and animal accommodation. Recent strain typing and other transmission studies have indicated that the agent responsible for nvCJD is identical to the BSE agent. It is too early to predict whether the cases of nvCJD seen to date herald a widespread epidemic. In any case, there is a need to provide guidance for health practitioners on the risks from humans infected with TSE agents.

Scope of this guidance

1.5 Health and safety law sets out a series of general duties on employers, employees and self employed people. There are specific regulations which cover work with biological agents such as TSEs, notably the Control of Substances Hazardous to Health Regulations 1994 (COSHH). These require employers to assess the risks in all cases where there may be exposure to biological agents. But the necessary containment and control measures will differ depending on whether there is a deliberate intention to work with the agent (such as in a research laboratory) or whether exposure is incidental to the work (such as in a hospital ward or operating theatre).

1.6 This guidance is therefore divided into three main sections as follows:

- hazards and risk associated with workplace exposure to TSE agents (including information on health and safety law);
- containment and control measures for experimental laboratory work with TSE agents, materials and infected animals (i.e. where there is deliberate intention to work with the agent);
- infection control of CJD and related disorders in healthcare settings (i.e. where any exposure to the agent is incidental to the work).

1.7 The purpose of this document is to provide guidance to employers on the precautions to minimise the exposure of employees and others to TSE agents from work activities. The guidance applies to many occupations that involve contact with people or animals infected with TSE agents, or potentially contaminated material. It should also be drawn to the attention of those responsible for advising others who may come into contact with TSE during the course of their work. Included in these two broad groups are:

- laboratory staff (including experimental animal house staff);
- healthcare workers (including infection control staff; medical and nursing staff particularly in neurology, ophthalmology, neuro- or ENT-surgery, oral and maxillofacial surgery, and dentistry; sterile services supply staff; and medical engineers);
- staff involved in hospice and community care;
- pathologists (including veterinary pathologists), histologists and post mortem technicians;
- funeral, cemetery and crematorium workers;
- local Consultants in Communicable Disease Control (CCDCs).

1.8 Additional advice for veterinary surgeons and those involved in the transportation, slaughtering and processing of cattle and cattle products can be found in a separate publication (BSE Background and general occupational guidance. ACDP. 1996). Guidance on handling meat and bone meal (MBM) material and an information sheet on occupational health risks from cattle, which will be of interest to farmers and others involved in animal husbandry, have also been published by the Health and Safety Executive. Details of these publications are given in the bibliography.

Box 1 Human and Animal TSEs

The human TSEs are:

- Creutzfeldt Jakob disease (CJD) including classical sporadic; familial; iatrogenic and new variant;
- Gerstmann Strussler Scheinker syndrome (GSS);
- fatal familial insomnia (FFI);
- kuru.

The human TSEs have a pre clinical phase that lasts for years. This is followed by rapidly progressive dementia, loss of memory and intellect, personality changes, or progressive unsteadiness and clumsiness. In CJD, sudden involuntary muscular jerking is frequently seen. In most cases, death occurs within a few months of onset of symptoms and the patient is usually mute and immobile in the terminal stages.

All human TSEs are very rare; the world wide incidence of CJD is about 1 per million people each year. The usual age of onset for classical sporadic CJD is late middle age (average age 63 years). About 85% of cases are classical sporadic; most of the rest are familial in origin. Some cases are the result of medical treatment (iatrogenic transmission). In March 1996, a new variant of CJD (nvCJD) was reported in 10 persons of unusually young age. It is characterised by behavioural changes, poor co ordination (ataxia), progressive cognitive impairment and often a relatively long duration of illness (up to 2 years). There are also characteristic changes in the brain with large accumulations of prion protein. Research findings published since March 1996 indicate that nvCJD and BSE are caused by the same infectious agent.

The other human TSEs (GSS and FFI) are exceptionally rare, affecting around 1 person in 10 100 million per year. Both appear to be inherited diseases and thus related members of a family may be affected. In GSS and FFI the disease is usually more prolonged than in CJD, and generally starts at an earlier age. GSS patients suffer predominantly from problems of balance and incoordination; FFI is characterised by abnormal sleeping patterns.

Kuru was found in the Fore tribe of New Guinea and was first reported in 1957. It was associated with funeral rites involving ritual contact with, preparation of, and consumption of the entire body including the brains of previous kuru victims. The establishment of a link between contact with infected tissue and the subsequent development of kuru first suggested an infective basis for all human TSEs. Occurrence of kuru has been markedly reduced following the abolition of cannibalism coupled with health education, although some cases may still arise from historical exposure.

There have been no confirmed cases of transmission of TSE by virtue of occupation. There have been a small number of reports of classical sporadic CJD in healthcare workers (including retired laboratory workers and a pathologist) but the link with their occupation is speculative. An excess of classical sporadic CJD has been found in dairy workers, but this is no higher in the UK than in other European countries which have not suffered the BSE epidemic. None of the cases of nvCJD have any obvious link with occupational exposure to BSE.

The animal TSEs are:

- scrapie in sheep, goats and moufflon;
- bovine spongiform encephalopathy (BSE) in cattle;
- transmissible mink encephalopathy (TME) in farmed mink;
- chronic wasting disease (CWD) in deer species;
- feline spongiform encephalopathy (FSE) in domestic cat and captive exotic felines;
- spongiform encephalopathy in captive exotic ungulates.

BSE was first confirmed in Great Britain in 1986. Up to December 1997 it has affected about 170,000 cattle in the UK and much smaller numbers in native-born cattle in Belgium, France, Luxembourg, Netherlands, Portugal, Republic of Ireland and Switzerland. A few cases have occurred in these or other countries following export of live cattle from the UK. Affected animals become unsteady on their feet, lose weight and become nervous hence mad cow disease. The BSE epidemic is in sharp decline as a result of the ban on feeding ruminant derived protein to ruminants. All animals suspected of having BSE are compulsorily slaughtered and completely destroyed.

Scrapie occurs in sheep, goats and moufflon, and has been recognised for more than 250 years. Affected animals often scrape themselves against objects to alleviate itching, become unsteady on their feet and lose condition. It is endemic in flocks in many countries, but there is no evidence that it can be transmitted to humans.

A disease similar to scrapie, TME has also occurred sporadically in farmed mink. CWD in Rocky Mountain elk, mule deer and some other deer species is also considered to be similar to scrapie. Neither have been reported in the UK. TSE has been recognised also in small numbers of domestic cats and captive, exotic felines and ungulates, most of which were born in the UK.

Part 2
Hazards and Risks Associated with Workplace Exposure to TSE Agents

Health and Safety Law

The Health and Safety at Work etc. Act 1974 (HSWA)

2.1 All work except domestic service is subject to regulation under the HSWA. **Employers** have general duties to ensure, so far as is reasonably practicable, the health, safety and welfare at work of employees, and to conduct their undertakings in such a way as to ensure, so far as is reasonably practicable, that other persons who may be affected by the work are not exposed to risks to their health and safety. **Self-employed** people have general duties to conduct their undertakings in such a way as to ensure, so far as is reasonably practicable, that they and other persons are not exposed to risks to their health and safety from the work. **Employees** have a general duty to take reasonable care for the health and safety of themselves and of other persons who may be affected by their work, and to co operate with their employer or any other person to enable them to comply with any health and safety duties.

The Management of Health and Safety at Work Regulations 1992 (MHSWR)

2.2 The MHSWR provide a framework for controlling health and safety at work. As well as calling for risk assessments, they also require employers to have access to competent help in applying the provisions of health and safety law; to establish procedures to be followed by any worker if situations presenting serious and imminent danger were to arise; and for co operation and co ordination where two or more employers or self employed persons share a workplace.

Genetically Modified Organisms (Contained Use) Regulations 1992

2.3 Experimental work involving the genetic modification of the *PrP* gene and the production of animals transgenic for the *PrP* gene, is subject to regulatory control under the Genetically Modified Organisms (Contained Use) Regulations 1992 (as amended). The Advisory Committee on Genetic Modification (ACGM) has prepared a Compendium of Guidance relevant to this type of work. Further information is available from the ACGM secretariat[1].

The Control of Substances Hazardous to Health Regulations 1994 (COSHH)

2.4 The COSHH Regulations provide a framework of actions designed to control the risk from a range of hazardous substances including biological agents. Schedule 9 of the COSHH Regulations specifically refers to biological agents which include the TSE agents. The essential elements of the COSHH Regulations are:

- risk assessment;
- prevention of exposure or substitution with a less hazardous substance (if the nature of the activity permits);
- selection of control measures;

- maintenance, examination and testing of control measures, e.g. protective equipment such as safety cabinets;
- provision of information, instruction and training for employees;
- monitoring exposure at the workplace (if a suitable procedure is available);
- health surveillance of employees (where appropriate, and if there are valid techniques for detecting indications of disease) when it can lead to action that will be of benefit to the health of employees.

2.5 The results of the assessment will assist in the selection of appropriate control measures. The primary requirement is to prevent exposure to a biological agent or substitute a safer biological agent, if this is practicable. Often these approaches will not be possible, and in such cases the risk of exposure should be minimised by the use of suitable control measures (see below and Parts 3 and 4).

2.6 The COSHH Regulations identify two broad categories of exposure to biological agents at work: (a) exposure which does not arise from the work but is incidental to it (e.g. healthcare, food production, sewage work) and; (b) exposure resulting from a deliberate intention to work with biological agents (e.g. laboratory research). A risk assessment should be made for both categories, but the scope for risk reduction and control may be less in the former category. Part 4 of this document gives guidance for healthcare work, where the exposure to TSE agents is incidental to the work. Information on work involving the slaughter and processing of cattle can be found in the general guidance on BSE (see bibliography).

The Reporting of Incidents, Diseases and Dangerous Occurrences Regulations 1995 (RIDDOR)

2.7 There is a requirement in RIDDOR for employers to report any infection reliably attributable to work with live or dead humans or animals, exposure to blood or body fluids or any potentially infected material derived from any of the above. There is also the need to report any accident or incident which resulted, or could have resulted, in the release or escape of TSE agents (or other biological agents) categorised in Hazard Group 3 or 4 (see paragraph 2.19). See also accident reporting and health surveillance below. Further information can be obtained from the Health and Safety Executive.

Local safety policies and codes of practice

2.8 There is a need to ensure that all employees have a clear understanding of any identifiable risks to their health arising from work, and the actions to be taken in dealing with situations in which exposure may occur. Under the COSHH Regulations employers must provide suitable and sufficient information, instruction and training on the risks and precautions to be taken. Under the MHSWR, they must provide comprehensive and relevant information on the risks and preventative and protective measures, together with adequate health and safety training. Local codes of practice may form part of this process of information, but thorough instruction on their day to-day application is needed in order to make them work effectively.

2.9 Specific information on the arrangements for working safely day to day can best be set out in local codes of practice. Employers have a responsibility to make the policy and codes freely accessible, either by putting them on display or by individual issue. All staff, including all newcomers and temporary workers, must be made aware of them.

2.10 Employers have a duty to consult employees on health and safety matters. Further information and details of additional guidance can be found in the leaflet Consulting Employees On Health And Safety: A guide to the law (HSE 1996).

Accident reporting and health surveillance

Accident reporting and recording

2.11 An official local record should be made of all accidents and occurrences with infectious or potentially infectious material involving the exposure of individuals. This applies whether or not the accident is reportable under RIDDOR.

List of employees exposed to human TSE agents

2.12 If a TSE were to develop as a result of occupational exposure, it may only become apparent decades later. Paragraph 11(1) and 11(3) of Schedule 9 of the COSHH Regulations require employers to keep a list of employees exposed to human TSE agents for 40 years following the last known exposure. Such a list is only necessary when there is a deliberate intention to work with the agent or in cases of incidental exposure if a risk assessment shows that there is a significant risk. For routine clinical care of patients with CJD or a related disorder however, this should not be necessary. It is often sensible to duplicate the relevant information with the individuals health record (see paragraphs 2.14 and 2.15 below).

Health surveillance

2.13 Where it is appropriate for the protection of the health of employees, both MHSWR and COSHH Regulations require that employees are under suitable health surveillance. Under MHSWR, health surveillance must be provided as appropriate, having regard to the risks identified by the risk assessment. Under COSHH Regulations, health surveillance must be provided where: there is an identifiable disease or adverse health effect that may be related to exposure in the workplace; there is a reasonable likelihood that the disease or effect may occur under the particular conditions of work; and there are valid techniques for detecting indications of the disease or effect.

2.14 In view of the difficulties in detecting the early indications of disease, it should be sufficient to set up and maintain a health record as defined in the Appendix of the COSHH Regulations. This could supplement any list of exposed workers. Further information is in Regulation 11(3), Schedule 9, the COSHH General Approved Code of Practice and The Approved Code of Practice on Biological Agents.

2.15 Although not a legal requirement, individual exposure and health records may be of great value for future epidemiological investigations. It is recommended that the minimum information that should be recorded is the full name (and maiden name for women), date of birth, National Insurance number and dates of (relevant) employment. The information on exposure needs to be linkable to individuals, although not necessarily at individual level (i.e. it may be that an indication of representative work can reasonably be applied to all those working in that area). Records should be kept for 40 years after the last known exposure. Regulation 11(4) requires that the records be offered to HSE if the employer ceases to trade before that time.

Risk Assessment

General principles

2.16 Employers must carry out a suitable and sufficient assessment of risks before any work involving potential risk to workers from a substance that is, or may be, hazardous to health. The assessment of risk required by the COSHH Regulations must be reviewed regularly and revised when conditions change, an incident occurs, a deficiency is noted or if, for any other reason, it is suspected that the assessment is no longer valid.

2.17 The risk assessment must include a review of all working procedures. For example, review of procedural controls, arrangements for the safe disposal of waste, the potential for the dispersal of infectious material in the working environment and the contamination of equipment and apparatus.

2.18 Factors that need to be considered in the risk assessment include:

i. whether there is a deliberate intention to work with the agent, or if any exposure would be incidental to the work (see paragraph 2.6 above);

ii. hazard categorisation of the agent (see Table 1);

iii. origin of the TSE agent;

iv. type of tissue handled (as this may indicate the likely level of agents present) (see Annex A);

v. knowledge of expression of the agent in any experimental model and whether the work is likely to result in a high titre

of infectivity;

vi. assessment of the type of task (e.g. concentration/purification);

vii. frequency of contact with the agents or materials likely to contain them;

viii. potential for inoculation injury in the workplace and other possible routes of exposure.

Hazard categorisation of TSE agents

2.19 The appropriate control measures for laboratory work with biological agents are determined largely by the Hazard Group classification of the agent. The EC Classification of Biological Agents establishes a list of biological agents as part of the Council Directive on the protection of workers from risks related to exposure to biological agents at work (90/679/EEC). Details can be found in the ACDP publication Categorisation of biological agents according to hazard and categories of containment and the 1998 supplement.

2.20 The classification is based on the risk of infection to a healthy worker using the well established criteria for four Hazard Groups. In determining the appropriate hazard grouping of a biological agent, note is taken of the pathogenicity (disease producing capability) of the organism to man, the hazard to laboratory workers, the potential for transmission to the community and the seriousness of any illness that might result after taking into account the availability of prophylaxis or effective treatment.

CJD and related diseases

2.21 CJD (including nvCJD), GSS, FFI and kuru cause disease in man which, once clinical signs appear, is invariably fatal and there is no effective prophylaxis or treatment available. However, apart from the rare examples of iatrogenic transmission, there is no evidence that CJD, or a related disorder, has been or can be spread from person to person by close contact, or has occurred in workers through occupational exposure. Furthermore, currently there is no evidence that nvCJD patients acquire their disease from occupational exposure. (A significant excess of CJD cases has been found among workers on dairy farms and on farms with a confirmed case of BSE. However, these cases have all been the classical type and not the nvCJD type. Strain typing of the agent causing CJD in farmers whose herds had confirmed cases of BSE showed that they were indistinguishable from classical CJD and distinct from nvCJD and BSE. The incidence of classical CJD in UK farm workers is no higher than in farm workers in other European countries which have not suffered from the BSE epidemic; the significance of this observation is unclear at present.)

2.22 The human TSE agents are classified in Hazard Group 3 because of the severity of infection. However, as it is recognised that the TSEs are unlikely to be transmitted by the aerosol route, derogation from full Containment Level 3 is allowed. This means that, subject to local risk assessment, certain containment measures may be dispensed with.

BSE and related diseases

2.23 BSE, and diseases in other species caused by the BSE agent (spongiform encephalopathy in felines and in captive exotic ungulates), are invariably fatal, once clinical signs have appeared, in the animals they affect. A link between BSE in animals and nvCJD in man has also been established, although there remain uncertainties about, for example, possible routes of exposure. BSE and related agents are now classified in the same Hazard Group as the agent responsible for CJD, i.e. Hazard Group 3 with derogation. Table 1 summarises the current position.

Scrapie and related diseases

2.24 Other animal TSEs (e.g. scrapie) are invariably fatal in the animals they infect, again once clinical signs have appeared. In view of the novel features of all TSE agents, and the uncertainty about infectivity in man, it is recommended that prudent precautions are taken when working with tissues or preparations from infected animals. However, as there is no evidence of transmission of scrapie to humans it is not formally classified as a biological agent or placed in a Hazard Group. Nonetheless, the recent amendment to Directive 90/679/EEC does include a footnote about animal TSEs, which recommends that

Containment Level 2 is sufficient for laboratory work with identified scrapie agents. It includes also a precautionary recommendation for Containment Level 3, with derogation applying, for work with TME and CWD. As none of these agents exhibit other hazards specified in the definition of a biological agent, such as allergenicity or toxicity, they are not covered by the COSHH Regulations. However, the MHSWR will apply, and a risk assessment is required by these regulations.

Origin of the TSE agent

2.25 It is usually more difficult, and sometimes impossible, to transmit a TSE agent to a different species at primary passage than to another member of the same species (assuming it is of the same prion protein (PrP) genotype). This is the species barrier effect, and is recognised by a shortening of the incubation period following a second passage in the new species. The transmission properties of the TSE agent are dependent on the host from which it is derived and on the passage history. For example, serial sub passage of scrapie agent in mice of different genetic make-up may select strains of agent with differences in incubation periods, infectivity and resistance to decontamination. Strain properties of cloned agents sometimes, but not always, alter following serial passage in a new species and re-isolation in the original species. Risk assessment needs to consider the species of origin as well as the species into which the TSE source has been passaged.

2.26 It is particularly important to consider carefully the risks from a TSE agent isolated from any species but which is subsequently passaged in non human primates or any genetically modified species expressing human or primate PrP (e.g. transgenic mice). Tissues from such animals should be treated as if they contained a TSE agent of human origin.

Distribution of TSE infectivity in tissues

2.27 Knowledge of which organs or systems are known to harbour the agent in natural disease is key to performing an adequate risk assessment; and subsequently in deriving suitable control measures to prevent or reduce the risk of occupational exposure to the agents, especially for laboratory work as this may involve contact with high titres of infectivity. However, data on tissue distribution of TSE infectivity are incomplete, and although studies are underway which will provide some additional information, there are likely to be significant remaining gaps in knowledge. The risk assessment needs to take into consideration these uncertainties. A summary of current information is given in Annex A, which will be particularly useful for risk assessments of experimental laboratory work. However, it is important that as further research results emerge these are incorporated into the risk assessment.

Sheep and goats

2.28 Bioassays in laboratory rodents have been used to investigate the tissue distribution of TSE infectivity in naturally occurring disease in sheep and goats. Present knowledge of this is given in Annex A, which presents data derived from studies on sheep and goats naturally infected with clinical scrapie. For simplicity, the data on sheep and goats have been combined. However, where minor differences between the sheep and goat data occur, the tissue concerned was placed in the highest category, e.g. pituitary gland would have been placed in the low infectivity category if based on the sheep data alone.

Cattle

2.29 The distribution of infectivity in bovine tissue is being studied in an on-going series of experiments. While early experiments concentrated on naturally infected, clinically affected field cases of BSE, subsequent studies have also addressed the distribution of infectivity in the pre-clinical stage using experimentally infected animals. The majority of studies have used parenteral inoculation of mice to determine whether infectivity was present in a range of tissues. While studies on naturally infected cases are complete, those on cattle that were experimentally exposed by mouth are still on-going. Interim results have been published in 1994 and 1998. In summary, it has so far been shown that:

- from naturally infected field cases the BSE agent has been detected only in brain, spinal cord and retina;
- a wide range of other tissues from naturally infected cattle has shown no detectable infectivity even though donor animals were clinically affected at the time of sampling;

- in cattle experimentally challenged with 100g of infected brain by mouth, infectivity was detected in the distal ileum from 6 months after challenge, becoming undetectable at 22 and 26 months post-challenge but then subsequently re-appearing. From shortly before clinical onset, which was at approximately 35 months post-challenge, infectivity became detectable in the brain, spinal cord, dorsal root ganglia (mid-cervical and mid-thoracic) and, at the time of writing, at one time point in the experiment in bone marrow. This was again in clinically affected animals.

2.30 Mice have been challenged orally also, but with a more restricted range of bovine tissues from confirmed cases of BSE. In these studies, only brain tissue has proved infectious to mice.

Humans

2.31 Limited information is available on the distribution of infectivity in human TSEs. Cases of accidental human to human (iatrogenic) transmission have been associated with the clinical use of human *dura mater*, cornea and hormones derived from human pituitary glands.

2.32 Lymphoid tissue (tonsils) in nvCJD cases has been found to contain the disease associated form of prion protein. However, the significance of this finding is not yet clear. It is possible that the distribution of infectivity of nvCJD is different from that of other forms of CJD, e.g. in the former there may be more involvement of lymphoreticular tissues possibly involving circulating lymphocytes. The assessment of risks from nvCJD should reflect this uncertainty, and will need to be revised as further research findings emerge about the pathogenesis of nvCJD.

2.33 Advice about clinical interventions on patients *known or suspected* to have CJD or related diseases and those *at risk* from CJD is given in Part 4.

Table 1
Summary of categorisation of the agents of TSEs[1]

Agents associated with:	Hazard Group[2]	Comments / Notations
Creutzfeldt-Jakob disease (CJD) including new variant CJD (nvCJD)	3	DE
Gerstmann-Strussler-Scheinker syndrome (GSS)	3	DE
Kuru	3	DE
Fatal familial insomnia (FFI)	3	DE
Bovine spongiform encephalopathy (BSE) and other related animal TSEs[3]	3	DE
Scrapie and other TSEs known not to be linked to BSE	-	These agents are not formally categorised[4]. See Part 3 for recommended laboratory precautions

1. This summarises the 1998 edition of the Approved List of Biological Agents which comes into force on 1 May 1998.

2. There is an exemption certification concerning the required containment measures for these agents. Full Containment Level 3 may not be necessary for all work with these agents. Further advice can be found in Part 3 of this guidance.
3. For the purposes of the hazard categorisation related animal TSEs include: Feline spongiform encephalopathy (FSE); spongiform encephalopathy (SE) in captive exotic ungulates; transmissible mink encephalopathy (TME); and chronic wasting disease (CWD). This category also includes BSE experimentally transmitted to other species.
4. The European Directive 97/65/EC on the adaptation of the European classification of biological agents includes the following footnote:

   There is no evidence in humans of infections caused by the agents responsible for other animal TSEs. Nevertheless, the containment measures for agents categorised in risk group 3(**) are recommended as a precaution for laboratory work,

except for laboratory work relating to an identified agent of scrapie, where Containment Level 2 is sufficient.

D: A list of workers exposed to these agents should be kept for 40 years following the last known exposure risk.

E: eye protection should be used for laboratory work.

[1]Secretary to the Advisory Committee on Genetic Modification, Health and Safety Executive, Rose Court, 2 Southwark Bridge. London SE1 9HS.

Part 3
Containment and Control Measures for Experimental Laboratory Work with TSE Agents, Materials and Infected Animals

Introduction

Scope

3.1 This section gives advice on the prevention and control measures for work involving the deliberate use of, or exposure to, TSE agents. It covers:

- all experimental work with preparations, body fluids or tissues known or likely to contain the agents of both human and animal TSEs;
- work with experimentally infected animals;
- work with preparations of purified prion proteins;
- any hosts or vectors in which TSE-associated material has been cloned by techniques of genetic modification and in which expression may be achieved.

3.2 The guidance and information given in this document is provided to help employers arrive at safe working practices, but it is emphasised that this does not negate the responsibility of the employer to carry out a full risk assessment of all individual work situations.

3.3 The COSHH Regulations employ a hierarchy of controls to prevent or, if this is not reasonably practicable, to control exposure to biological agents. The preferred method of control is to substitute a safer biological agent, or to use engineering controls for primary containment. Personal protective equipment, especially respiratory protective equipment (RPE), should always be seen as a last resort.

Basic precautions to avoid exposure

3.4 The use of basic hygiene precautions are generally applicable wherever there is a risk of exposure to potentially infected material. These are summarised in Table 2. In the context of TSEs, they are particularly important when the work may involve exposure to high or medium risk tissues (see Annex A, table A.1) from TSE infected individuals or animals or extracts prepared from them. Other measures may be required in certain occupational settings and there are, in any case, more stringent requirements under law for laboratory work with biological agents.

3.5 There is no evidence that the TSEs are transmitted by aerosols from contaminated material. Accidental ingestion should be readily avoidable by the use of basic hygiene measures. Where the agent is in high concentration and/or likely to be actively dispersed during, for example, some laboratory operations such as homogenisation of tissue, there might be a need to prevent inhalation and/or splashing of mucous membranes by the use of a microbiological safety cabinet or other primary enclosure.

Table 2
General basic protective measures
(see also Annex B for advice on cleaning, decontamination and waste disposal)

- Adhere to safe working practices, e.g. do not eat, drink, smoke or take medication in the laboratory; remove protective clothing and wash hands before leaving the laboratory.
- Protect skin wounds such as cuts, abrasions, eczematous lesions, e.g. by the use waterproof dressings.
- Wear appropriate protective clothing routinely, e.g. consider use of disposable gowns and aprons.
- Wear disposable gloves for all work with TSE material.
- If there is a possibility of splashing, protect eyes and mucous membranes - use eye protection or full face visor where appropriate.
- Avoid active uncontrolled dispersal of material - take care when mixing, centrifuging or homogenising material to avoid splashing. In the laboratory, use enclosed systems (e.g. sealed centrifuge buckets or, where appropriate, a microbiological safety cabinet).
- Avoid or minimise the use of sharps wherever possible (needles, knives, scissors and laboratory glassware) use plastic single-use disposable items (e.g. containers, pipettes, inoculating loops and other such instruments).
- Consider use of suitable hand protection, such as armoured glove(s) where use of sharp instruments is essential, e.g. in post mortem examinations or collection of human or animal brain/spinal cord.
- Record all accidents involving parenteral exposure to TSE material or contaminated wastes.

Experimental Laboratory Work

Containment of laboratory work with the TSE agents and associated materials

3.6 Those involved in laboratory work with biological agents should be familiar with the detailed advice on containment and control measures given in the 1995 ACDP publication Categorisation of biological agents according to hazard and categories of containment. It is not the intention to re-iterate that advice here but to highlight those aspects which are particularly relevant for work with TSEs, and to give guidance on the meaning of derogation in this context.

3.7 The Containment Level at which a biological agent is to be handled usually corresponds with its categorisation, but this may not necessarily be the case for TSE agents because of their unique features. The Hazard Group of the agent forms the basis of a risk assessment to determine the appropriate containment and control measures.

3.8 The main precautions that must be emphasised for laboratory work with human or animal TSEs are:

- a high standard of information, instruction and training for staff, together with effective supervision;
- the laboratory should be dedicated to TSE work and separated from other activities taking place in the same building;
- due to the unusual resistance properties of TSE agent, special decontamination procedures are required (see Annex B);
- because of the need for special decontamination procedures, single-use disposable items or dedicated equipment should be used wherever practicable. In the case of large items this could be interpreted as specified parts of the item, e.g.

dedicated ultracentrifuge rotors or electron microscope grids;

- access is restricted to authorised individuals.

3.9 Based on the current Hazard Categorisation of the TSE agents, the recommended overall Containment Levels are given in Table 3. For some work derogation from full Containment Level 3 may be allowed, but this will depend on the nature of the work and the results of the local risk assessment.

Table 3
Containment Levels recommended for experimental work with the agents of TSEs

Laboratory work with:	**Overall Laboratory Containment Level**	**Animal Containment Level**
Human TSE agents[a]	**3**[b]	**3**[b] for small animal work
BSE and other related animal TSE agents (FSE, SE in captive exotic ungulates TME and CWD[d])		**1** for large animal work[c]
Scrapie[d]	**2**	**2** for small animal work **1** for large animal work[c]

Notes

(a) This includes primary sources and any sub-passages of human derived agents in other species. The inclusion of work with any animal TSE agents passaged in primates or in genetically modified mice with the human PrP gene should also be considered. The containment measures apply to experimental work with tissues or preparations unless they are known not to contain infectivity.

(b) Subject to local risk assessment, derogation from full Containment Level 3 may be applied, see paragraph 3.11.

(c) The risk of exposure to TSE agents from large intact animals (e.g. sheep or cattle) is considered to be remote and therefore Containment Level 1 is generally considered appropriate for experimental work with large animals. Smaller animals (e.g. mice) generally present a higher risk of biting or scratching and should usually be handled at the Containment Level equivalent to the Hazard Group of the agent.

(d) The European Directive 97/65/EC on the adaptation of the European classification of biological agents includes the following footnote:

There is no evidence in humans of infections caused by the agents responsible for other animal TSEs. Nevertheless, the containment measures for agents categorised in risk group 3(**) are recommended as a precaution for laboratory work, except for laboratory work relating to an identified agent of scrapie where Containment Level 2 is sufficient.

Human TSEs, BSE and other animal TSEs (except scrapie)

3.10 For work with the TSE agents classified in Hazard Group 3 (agents of CJD, GSS, kuru, FFI, BSE and related TSEs) it may not always be appropriate to work in conditions that relate strictly to the hazard grouping. Transmission of TSEs is thought most likely to occur by the percutaneous route, and to a lesser extent by ingestion, so derogation from full Containment Level 3 may normally be permitted, subject to local risk assessment. The TSEagents classified in Hazard Group 3 are specified in the exemption certificate accompanying the 1998 edition of the Approved List.

Derogation from Containment Level 3

3.11 The following derogations from full Containment Level 3 may be considered as part of any risk assessment process for work with TSE agents classified in Hazard Group 3.

Negative air pressure

Subject to local risk assessment, it may not be necessary to maintain the laboratory at an air pressure negative to atmosphere, as would normally be required for work at Containment Level 3. However, if the laboratory is mechanically ventilated, it must be maintained at an air pressure negative to atmosphere while work is in progress. In practice, when in use, the air flow through a microbiological safety cabinet will usually mean that the laboratory is maintained at negative pressure.

Sealability

The TSE agents are largely unaffected by normal fumigants, therefore, for the purposes of TSE containment, there is little practical benefit to be gained by making the laboratory sealable for fumigation. However, the local assessment should consider what decontamination methods would be used, particularly in the event of a major spillage.

HEPA filtration

Where a laboratory is mechanically ventilated, it may not be necessary for all extract air to be HEPA filtered, subject to local risk assessment. (Any air exhausted through a microbiological safety cabinet would in any case be HEPA filtered).

Scrapie

3.12 Work with the agent of scrapie can be conducted at lower levels of containment. Containment Level 2 is considered sufficient for experimental work involving tissues from scrapie infected animals. Special attention should be given to the use of dedicated equipment where practicable and the application of special decontamination requirements (see Annex B).

Work with disrupted tissues and concentrated TSE agents

3.13 There may be experimental situations where the amount of TSE agent is likely to be significantly higher than levels normally encountered in naturally occurring disease. The risk of exposure may also be increased when tissue known to carry TSE infectivity is disrupted or concentrated (e.g. by homogenisation and centrifugation procedures). Such operations should be appropriately assessed and contained. Modified containment with additional precautions may be required on the basis of a local risk assessment. For example, the derogations from Containment Level 3 suggested above may not be appropriate for such work with CJD infected material.

Research work with animals

Containment of animals experimentally infected with TSE

3.14 Detailed guidance on handling infected animals can be found in the publication Working safely with research animals: management of infection hazards (ACDP 1997). It supplements the guidance in the Categorisation of biological agents according to hazard and categories of containment (ACDP 1995).

3.15 In general, live animals infected experimentally with TSEs do not pose a significant risk of exposure to TSE agents. However, because of the possibility of maternal transmission, parturient animals infected with TSE agents should be safely isolated and the non-viable products of parturition and other contaminated material destroyed by incineration. A local risk assessment should be made and local rules drawn up to ensure worker safety. The principles of safe working practice, including handling and restraint of animals by fully trained staff, good husbandry, basic hygiene precautions and the use of appropriate

personal protection apply.

3.16 Derogation from full Containment Level 3 may be considered for experimental work with live animals inoculated with TSE agents in Hazard Group 3. The following broad principles for assigning containment may be considered, subject to a local risk assessment:

> **For small animals** (e.g. rodents, rabbits, cats, dogs) Animal Containment Level 3 with derogations is generally acceptable. The derogated measures are the same as those for laboratory work (paragraph 3.11) except that the requirement for negative air pressure may be balanced by the need for positive pressure for animal husbandry purposes In such cases the use of simple engineering controls (e.g. flexible barriers) or RPE may be necessary and should be carefully considered in the local risk assessment. In cases of doubt, further information can be obtained from HSE.
>
> Animal Containment Level 2 is considered sufficient for small animals inoculated with the scrapie agent, with the proviso above about the need to balance the requirements for inward air flow against the need for positive pressure.
>
> **For large domestic animals** (e.g. sheep and cattle) Animal Containment Level l is normally sufficient. However, to prevent cross-contamination and/or cross-infection, local guidelines may insist on a higher level of isolation and containment. Additional measures may be required in particular circumstances, for example, if there was a risk of exposure from bites, scratches, abrasions or contact with fluids or tissues, additional containment precautions would be required.
>
> Animal Containment Level l is considered adequate for large animals inoculated with the agent of scrapie.

3.17 The preferred method of disposal of carcasses and other waste materials from all animals experimentally infected with TSE is incineration. Bedding and faeces from large animal accommodation should be incinerated if the results of the assessment indicate that TSE infectivity may be shed (e.g. for a period following oral challenge). After the initial shedding phase it can be disposed of in the normal way (e.g. by landfill burial or discharge to the sewer system) subject to the requirements of MAFF and the Environment Agency.

3.18 Additional containment precautions need to be considered for procedures and experiments where the following special circumstances apply:

- concentrations of infectivity above those found naturally could be expected;
- routes of inoculation are used in which leakage of infectious material externally could occur, or during the oral dosing phase when the feed material remains exposed;
- there are other experimental circumstances that might enable external release of infectivity;
- experiments with genetically modified animals.

Post mortem examination of animals with TSE

3.19 Before post mortem examinations are performed on animals with natural or experimental TSE, a risk assessment must be carried out to establish whether it is appropriate to do a post mortem (i.e. can exposure be prevented) and to assess the appropriate level of containment and controls necessary for the procedure. The principles described above for derogation from Containment Level 3, and the use of additional precautions where necessary, apply here also. The following procedures for small animal post mortem should serve as a guide to drawing up local codes of practice. If it is necessary to undertake a large animal post mortem, it is recommended that specialist expert advice is sought from the Health and Safety Executive.

3.20 Basic precautions for small animal post mortems:

i. ensure that the Containment Level of the post mortem area is appropriate for the agent involved. Where it is not possible to use a dedicated room, an area of the post mortem room should be set aside;

ii. consideration should be given to the subsequent disinfection of working surfaces, for example, work may be conducted in a stainless steel or enamel tray which can then be autoclaved. Other working surfaces should be protected by disposable coverings;

iii. the procedure should be planned so that all equipment required is readily to hand and work should be organised so that there are no interruptions (e.g. to answer the telephone);

iv. single-use disposable items should be used wherever practicable; alternatively a set(s) of dedicated instruments may be used;

v. protective clothing including gloves, gowns, masks and visors or safety spectacles should be worn;

vi. a clean assistant should be available to take care of record-keeping, and handing over instruments etc;

vii. procedures for disinfection and decontamination as described in Annex B should be followed.

Animal neuropathology

3.21 Neuropathological examination of unprocessed experimentally infected animal TSE material (except scrapie and related agents) should be conducted at Containment Level 3. Precautions must be taken to prevent dispersal of infected material. Extra care will be needed to avoid penetrating injuries, and eye protection should be used to avoid splashing on to the conjunctiva. Autoclaving and disinfection procedures should be as recommended in Annex B. Further guidance on the decontamination of formalin fixed tissue for neuropathology is also given in Annex B.

Use of bovine eyes in research

3.22 Infectivity has been detected in the retina taken from animals clinically affected with BSE. There is a potential risk that researchers working with bovine eyes from apparently healthy cattle may be handling material containing BSE infectivity.

3.23 As a precautionary measure, eyes from healthy animals over 6 months of age are subject to the Specified Bovine Material Order 1997. Before collection, prior approval should be sought in writing from the Regional Manager of the Meat Hygiene Service.

3.24 If research work with bovine eyes is essential, it is recommended that standard basic precautions to prevent infection are strictly adhered to (see Table 2). If a choice can be made, it would be preferable to use eyes from beef breed calves less than 6 months old. If the eyes are from animals known or suspected of being infected with BSE, the earlier recommendations for work with BSE must be adopted (see Table 3).

Part 4
Infection Control of CJD and Related Disorders in the Healthcare Setting

Introduction

Scope

4.1 This section provides advice on safe working practices to prevent the transmission of CJD and related disorders in hospital and community healthcare, diagnostic laboratory, and post mortem room settings. Whilst the evidence to date does not suggest that CJD and related disorders are spread from person to person by close contact, it is known that transmission can occur in specific situations associated with medical interventions (known as iatrogenic infections). A number of cases of CJD have been associated with the administration of hormones prepared from human pituitary glands and *dura mater* preparations, and three cases have been reported associated with corneal grafts. Iatrogenic transmission has also been identified following neurosurgical procedures with inadequately decontaminated instruments. Consequently, there are particular groups of patients who present a greater risk of potential exposure to the CJD agent for attending healthcare staff. Likewise, there are specific occupations which place the worker at a greater exposure risk, e.g. neuropathologists and those workers involved in *post mortem* examination of known or suspected CJD cases.

4.2 This section also includes and updates earlier advice from the Department of Health on preventing iatrogenic transmission.[2,3] It also provides guidance aimed at preventing the remote possibility of transmission of infection from patients to healthcare workers. The occupational infection control advice issued to *post mortem* rooms and anatomy departments given in the Department of Health circular, PL(94)CO/2, remains current and should be followed where appropriate (copies available from the Department of Health). This circular advises anatomy departments not to accept for teaching or research purposes bodies or brain, spinal cord or eyes from donors currently identified as being at higher risk from developing CJD or a related disorder (see Table 4). It suggests questions which might be used by anatomy departments when formulating their own guidance on exclusion criteria for prospective donors, e.g. whether the patient showed signs of dementia or other progressive neurological defect.

Patient confidentiality

4.3 There has been increased media and press interest in patients suffering from CJD, and whilst it is important that staff are aware of the risks so that appropriate precautions can be taken, healthcare staff are reminded of the need to maintain patient confidentiality and to avoid unnecessary disclosure of patient names and clinical details. For example, the use of a code number rather than a name on clinical samples could be considered.

Standard infection control procedures

4.4 The epidemiological evidence to date does not suggest that, in the majority of situations, there is need for particular precautions beyond those used for other patients. Guidance on the management of infection control in hospitals and residential and nursing homes has been published previously (see bibliography). This guidance is not re-iterated here, but it is emphasised that the use of routine standard infection control practices will minimise the exposure of individuals involved in the healthcare of patients who have, or may develop TSE, and protect them from the very remote possibility of infection. An important aspect of this is to ensure that the appropriate procedures are being adhered to. Employers and managers will therefore need to ensure

that effective management systems are in place. Guidance on the management of health and safety in the health services has been prepared by the Health Services Advisory Committee (see bibliography).

Occupational exposure

4.5 Currently there is no evidence of any specific occupational risk of transmission. However, available information is limited and, as CJD remains a rare disease, it is not possible to draw firm conclusions. It is prudent therefore to take a precautionary approach. Within the general healthcare setting, workers from a range of occupational groups may potentially be exposed to tissues from patients *known or suspected* to have CJD, or those who may be *at risk* of developing CJD, that may contain the agents responsible for CJD or related disorders. Therefore, any healthcare worker who attends patients in these groups, and might come into contact with tissues that may contain the CJD agent, should be aware of the risks of exposure.

Patient risk groups (referred to below as *known, suspect or at risk* patients)

4.6 When considering measures to prevent transmission to patients or staff in the healthcare setting, it is useful to make a distinction between those patients who are *known or suspected* to have CJD or a related disorder, i.e. those with clinical symptoms, and those who are potentially *at risk* of developing one of these diseases, i.e. asymptomatic, but having a clinical or family history which places them in one of the risk groups. Table 4 sets out these groups in more detail. It is important to note that the requirements set out below apply only to the relatively small number of patients in the risk groups.

4.7 In most routine clinical contact, no additional precautions are needed for the care of patients in the risk groups. However, when certain invasive interventions are performed there is the potential for exposure to the agents of TSE. In these situations it is essential that control measures are in place to prevent the iatrogenic transmission of TSE. The tissues that present the highest risk of exposure to the agents of TSE are the **brain, spinal cord, and eyes**. Therefore, special precautions need to be taken for interventions involving these tissues for *known, suspect or at risk patients*, i.e. all the groups identified in Table 4. Furthermore, special precautions need to be considered for **all** clinical interventions on *known or suspect* patients. This is partly because *known or suspect* patients will, by definition, have clinical symptoms, and therefore there may be a greater likelihood of the infectious agent being present in their tissues, but most importantly because of the added uncertainties about the tissue distribution of the agent in cases of nvCJD. Specific advice on clinical procedures for the various patient risk groups identified in Table 4 is given in paragraphs 4.21-4.36, and is presented as a flow chart on page 35.

Table 4
Patient Risk Groups

Known or suspect patients	***At risk patients***
Patients **diagnosed** as having CJD or a related disorder*	Asymptomatic patients who are **potentially** at risk of developing CJD or a related disorder*:
Patients **suspected** of having CJD or a related disorder* i.e. whose clinical symptoms are suggestive of CJD but where the diagnosis has not yet been confirmed.	- recipients of hormone derived from human pituitary glands, e.g. growth hormone, gonadotrophin; - recipients of human *dura mater* grafts; - people with a family history of CJD, i.e. close blood line relatives (parents, brothers, sisters, children, grandparents and grandchildren).

* ie. classical sporadic CJD, nvCJD, GSS, FFI and kuru

4.8 It has been noted already that nvCJD is quite distinct from classical forms of CJD. This difference appears to extend to the pathogenesis of the disease, and it has been suggested that in nvCJD there is more involvement of lymphoreticular tissues

possibly involving circulating lymphocytes. The risk tissues may therefore need to be redefined as further research findings emerge and as the estimation of the numbers of nvCJD cases becomes clearer. At present, the number of people incubating nvCJD is not known.

4.9 Transfusions of whole blood, component blood or blood derivatives have not been shown to transmit the classical CJD agent. However some experimental evidence suggests that intracerebral inoculation of some blood components can occasionally transmit the CJD agent. Further studies are in progress to investigate these findings. To avoid the theoretical possibility of transmission of CJD by transfused blood, recipients of human growth hormone were excluded from donation in 1989, and recipients of other human-derived pituitary hormones excluded since 1993. Work is underway to assess the risk of transmitting nvCJD by blood transfusion and, in the interim, the National Blood Authority is working towards the possible extension of leucodepletion of blood as a precautionary measure.

Hospital Care

4.10 The following advice is for those involved in the care of patients *known, suspect or at risk* of developing CJD or related disorders. This advice should be taken into consideration in the development of local infection control policies. The responsibilities for infection control policies should be clearly defined locally in line with existing Department of Health guidance (HSG(95)10, see bibliography for details). In general, this will be the responsibility of the infection control team.

Ward Procedures

4.11 Available epidemiological evidence suggests that normal social or routine clinical contact with a CJD patient does not present a risk to healthcare workers, relatives and the community. Isolation of patients with CJD is not considered necessary, and they can be nursed in the open ward with no particular precautions beyond the routine infection control used for all other patients.

4.12 The distribution of TSE infectivity in natural disease has been discussed earlier. In the main, most infectivity is likely to be concentrated in the central nervous system (CNS), and particular care should be taken with such specimens from *known, suspect or at risk* patients. For example, use disposable gloves, aprons and single-use disposable instruments when performing a lumbar puncture for the collection of cerebrospinal fluid (see sample collection below). It is important to ensure that only trained staff, aware of the hazards, should carry out such procedures. At present, there is no evidence of infectivity in saliva, body secretions or excreta and, therefore, any potential exposure to these body fluids should be handled as for any patient, i.e. treated as potentially infectious in line with standard infection control procedures. As mentioned previously, there are uncertainties about the risks of TSE transmission from blood. However, careful attention to standard infection control procedures will minimise any such risk.

4.13 Drug administration by injection and the collection of blood specimens should involve the precautions used for all work of this type with any patient, i.e. avoidance of sharps injuries and other forms of parenteral exposure, and the safe disposal of sharps and contaminated waste by incineration. Again, these procedures should be carried out by trained personnel aware of the hazards involved.

4.14 In the event that a *known, suspect or at risk* patient becomes pregnant, childbirth should be managed using standard infection control procedures. The placenta, other associated material and fluids should be treated as if infected, and disposed of as infectious clinical waste by incineration, unless they are needed for investigation, in which case the precautions for dealing with infected tissue should be followed (see below). Instruments should be handled following the advice below on clinical procedures.

4.15 Used or fouled bed linen (contaminated with body fluids or excreta), should be removed from the bed and washed and dried in accordance with current practice and advice (Department of Health HSG(95)18, see bibliography). No further handling or processing requirements are necessary.

4.16 Spillage in the ward of potentially CJD-infectious materials should be removed using absorbent material, the surface disinfected with an appropriate disinfectant, and any waste disposed of as clinical waste by incineration. Disposable gloves and an apron should be worn when removing such spillage(s) and disposed of by incineration. See Annex B for further advice on disinfection.

4.17 Waste material should be handled as for all clinical waste, and disposed of by incineration in line with standard practice Safe disposal of clinical waste. HSAC 1992. New edition due mid-1998).

4.18 Any accident involving sharps, or contamination of abrasions with blood or body fluid, should be gently encouraged to bleed, gently washed (avoid scrubbing) with warm soapy water, rinsed, dried and covered with a waterproof dressing, or further treatment given appropriate to the type of injury[4]. Splashes into the eye or mouth should be dealt with by thorough irrigation. The accident should be reported to the accident supervisor and an accident or incident form completed. See also the section on page 8 on accident reporting and health surveillance.

Sample collection and labelling

4.19 Biopsy and lumbar puncture samples from *known, suspect or at risk* patients should only be taken by trained personnel who are aware of the hazards involved. Disposable gloves and eye protection should be worn where splashing may occur. Samples should be marked with a Biohazard label and, because of the increased media interest in CJD, particular consideration should be given to the need to maintain patient confidentiality. For example, the use of a code identifier rather than labelling with the patient name might be appropriate.

4.20 Because of the unusual resistance of the TSE agents, single-use disposable equipment should be used wherever practicable, and all small items contaminated by such specimens destroyed by incineration. Where this is not possible, the advice in Annex B on decontamination should be followed.

Clinical procedures

General measures

4.21 The use of standard infection control procedures during any clinical intervention will reduce the risk of infection. There are particular concerns regarding surgical and other clinical procedures on *known, suspect or at risk* patients because of the potential for onward transmission to other patients via contaminated surgical instruments. The following guidance should also serve to protect healthcare staff involved in such clinical procedures.

4.22 For the care and clinical management of *known, suspect or at risk* patients it may be necessary to undertake a range of clinical procedures. In these situations every effort should be made to plan carefully not only the procedure, but also the practicalities surrounding the procedure, e.g. instrument handling, storage, cleaning and decontamination or disposal. It may be useful to plan that the patient is last on the days operating list. No other discrimination should be permitted.

4.23 For non-invasive investigations, e.g. certain imaging or X-ray procedures, no specific precautions, other than those that would normally be applied to safeguard patient well-being are required.

4.24 Whilst the risk of transmission of infection via surgical or clinical procedures is generally accepted as small, there is still a need for specific precautions when undertaking certain procedures on *known, suspect or at risk* patients. This will depend first on whether the patient is symptomatic, i.e. *known or suspected* of having CJD, or non-symptomatic but falls into one of the at risk categories. The second consideration is about the type of procedure. In general, for *known or suspect* patients, whatever the clinical procedure, disposal of all instruments is recommended. Whereas, for *at risk* patients, disposal is recommended only where there is contact with a high risk tissue, i.e. brain, spinal cord or eye, and less stringent precautions are generally acceptable when there is contact with other tissues which are unlikely to contain the agent of CJD. This is illustrated by the algorithm chart on page 35.

4.25 All staff directly involved in procedures on patients in the risk groups, or in the subsequent re-processing or disposal of potentially contaminated items, should be aware of the specific precautions, and adequately trained. These staff should also be made aware of any clinical intervention in sufficient time to allow the necessary preparations for the procedure; this should include notification to the Sterile Services Department (SSD) or re-processing units, where appropriate. This will also allow time to obtain the most suitable instruments and equipment, which may not be those used routinely. Single-use items or components, such as patient circuits used in renal support equipment, should be used wherever possible.

Precautions during clinical procedures on known or suspect patients

4.26 The following precautions should be taken for all clinical procedures on known or suspect patients:

- wherever appropriate and possible, the intervention should be performed in an operating theatre;
- where procedures are performed at the bedside, e.g. a lumbar puncture, care should be taken to ensure the environment may be readily cleaned should a spillage occur (see Annex B). The protective clothing described below should be worn by the healthcare personnel performing diagnostic procedures;
- perform the procedure at the end of the list to allow normal cleaning of theatre surfaces before the next session;
- involve only the minimum number of healthcare personnel required;
- wear the following single-use protective clothing:

  -liquid repellant operation gown, over a plastic apron

  -gloves

  -mask

  -visor or goggles;

- maintain a one-way flow of instruments;
- use single-use disposable surgical instruments and equipment where possible.
  Note: If single-use disposable items are not available the instruments should **under no circumstances** be re-used;
- destroy **all** used instruments and protective clothing by incineration.
  Note: Instruments that will not be entirely destroyed by incineration should be subject to a process to ensure surface decontamination. These items may then be considered fit for disposal via landfill.

4.27 Some expensive items of equipment, such as drills, may be prevented from being contaminated by using shields, guards or coverings, so that the entire items do not need to be destroyed. The drill bit, other parts in contact with high risk tissue, and the protective coverings would then need to be incinerated. However, in practice, it may be difficult to ensure effective protective covering, and advice should be sought from neurosurgical staff and the manufacturer to determine practicality. For example, the screws of neurosurgical stereotactic frames, which are placed in the cranium, should be considered as being in contact with high risk tissue and therefore should be destroyed. However, there is a potential risk of the frame being contaminated as the screws are removed through it, therefore the frame should also be discarded.

4.28 Instruments that have been used on a suspect CJD patient, e.g. to take biopsy material for diagnosis of CJD, may be quarantined by securely storing in a rigid, sealed container after use, until the diagnosis is confirmed. If the case is confirmed as CJD, or if after testing the diagnosis remains suspected CJD, the instruments should be disposed of by incineration. Only if a definitive alternative diagnosis is confirmed may the instruments be cleaned and decontaminated following the usual routine procedures.

Precautions during clinical procedures on at risk patients

4.29 If the clinical intervention involves **brain, spinal cord, or eyes**, the precautions recommended above for procedures on known or suspect patients should be taken.

4.30 If the clinical intervention **does not involve brain, spinal cord, or eyes**, the following precautions should be taken:

- wear the following protective clothing (i.e. the same as above but may be re-processed if not designated single-use):

-liquid repellant operation gown, over a plastic apron

-gloves

-mask

-visor or goggles;

- use single-use surgical instruments and equipment wherever reasonably practicable;
- destroy all single-use items by incineration;
- re-usable surgical instruments and equipment must not be re-used until one of the recommended decontamination procedures has been carried out (see Annex B).

4.31 Where there is no exposure to high risk tissues, instruments which are not single-use can be re-processed as described in this guidance, providing that they are able to tolerate the process (e.g. stainless steel surgical instruments such as forceps, cutters, retractors).

Labelling and transportation of instruments

4.32 All instruments and items of equipment that have been in contact with *known, suspect or at risk* patients should be clearly identified. Items used on *known or suspect* patients should be labelled for disposal. Items used on *at risk* patients, where there has been contact with brain, spinal cord or eye, should also be labelled for disposal, whilst those used on other tissues should be labelled either for re-processing or disposal as appropriate.

4.33 Items for re-processing should be securely contained in a robust, leak-proof container, and transferred to the re-processing unit or SSD as soon as possible after use. Items should be transferred to the reprocessing unit by a designated person from the theatre team.

4.34 Items for disposal by incineration should be isolated in a rigid clinical waste container and transported to the incinerator as soon as practicable, in line with the current disposal of clinical waste guidance.

Cleaning and decontamination

4.35 The nature of the agents of TSEs is such that standard methods such as autoclaving cannot be relied upon to inactivate the agents completely. The emphasis must, therefore, be on removal of the agents by thorough cleaning, followed by an appropriate decontamination process. Detailed advice on cleaning and decontamination is given in Annex B. However, this does not apply to instruments that have been used in procedures on *known or suspect* patients, or those used on *at risk* patients where there has been contact with brain, spinal cord or eye, as these items must be disposed of by incineration.

Instrument use on subsequent patients

4.36 After decontamination as described above, surgical instruments (if incineration is not required) should be put through the standard hospital procedures for re-processing instruments, i.e. cleaned again, inspected, function tested, packed and sterilized, before being made available for use on another patient.

[2]DA(81)22 and DA(84)16 "The management of patients with spongiform encephalopathy (Cruetzfeldt-Jakob Disease CJD)", 1981 and 1984, Department of Health and Social Security.

[3]PL(92)CO/4 "Neuro and ophthalmic surgery procedures on patients with or suspected to have, or at risk of developing CJD or GSS", 1992, Department of Health.

[4]The use of concentrated disinfectants and/or surgical excision of the site of exposure has been suggested (Aguzzi and Collinge *Lancet* 1997). However, because of the lack od data at this stage, these views were not

supported by the working group, but the situation will be kept uder review.

Diagnostic Laboratories

Routine laboratory work

4.37 A range of laboratory tests may be required for the clinical management of *known, suspect or at risk* patients, for example routine biochemical, haematological or microbiological analyses. The classification of the agent of CJD has been discussed earlier and, because it is classified in Hazard Group 3, all clinical specimens from *known, suspect or at risk* patients should be handled at Containment Level 3. However, the option of derogation does apply and, based on local risk assessment, certain Containment Level 3 precautions can be dispensed with.

Samples from at risk patients

4.38 From information about the tissue distribution of infectivity of TSEs, it is thought that samples from the CNS present a greater risk of exposure to the agent of CJD than other samples. For routine clinical analysis not involving deliberate intention to work with the agent of CJD, samples from *at risk* patients that are not from the CNS, and are not known to be contaminated with CNS, can generally be handled in the same way as other clinical samples, providing that the risks have been assessed as required by the COSHH Regulations. In general, blood, urine, faecal specimens and swabs can be collected, processed and handled as for any other patient. General guidance on the handling and disposal of clinical specimens has been issued by the Health Services Advisory Committee (1992) and is currently being updated.

Samples from known or suspect patients

4.39 When handling specimens from *known or suspect* patients, or CNS specimens from *at risk* patients, particular care should be taken to avoid accidental inoculation or injury, for example, when preparing samples for microscopy or culture. Wherever practicable, disposable equipment should be used (cell counting chambers etc.) and items contaminated by the specimens should be destroyed by incineration, or else autoclaved or disinfected to the required standard (see Annex B). Special arrangements may be needed to minimise any residual contamination of equipment. Where manual analysis using disposable equipment is not feasible, and automated equipment is to be used, the potential for residual contamination must be considered and be dealt with appropriately before equipment is serviced. Where stringent decontamination procedures are inappropriate, as in the case of microscopes, the equipment should be cleaned and regularly maintained to avoid accumulation of potentially contaminated debris.

Neuropathology specimens

4.40 The general precautions above for handling specimens apply for similar work with brain and neural biopsy specimens from *known, suspect or at risk* patients. However, as infectivity may be concentrated in such CNS samples, they present a greater risk of exposure, and additional precautionary measures are appropriate. It may be more appropriate for such specimens to be handled in a specialist neuropathology laboratory or centre. Where there are facilities locally, limited histological processing can be undertaken with care by staff taking suitable precautions and wearing the appropriate protective clothing etc. For the specialist laboratory handling large numbers of samples, additional precautions may be necessary because of the possibility of increased residual contamination.

4.41 All preparations of brain and neural tissue from *known, suspect or at risk* patients for diagnosis and confirmation must be treated as potentially infectious, and handled in the laboratory at Containment Level 3 (subject to derogation, see Part 3). The use of disposable non permeable material is a convenient way of preventing contamination of the work surface. This covering and all washings, other waste material and protective clothing should be disposed of by incineration.

4.42 For optimal fixation of whole brain for general histopathology purposes, standard formalin should be used. However,

formalin-fixed TSE tissue retains infectivity for long periods, if not indefinitely, and should be handled with the same precautions as fresh material. Similarly, tissue for electron microscopy fixed in glutaraldehyde retains its infectivity. This is of equal importance when handling archive material stored in fixative, blocks or as mounted slides. As evidenced by work with both CJD and scrapie, formalin-fixed TSE tissues can be decontaminated largely, if not completely, by formic acid treatment. However, as the full extent of the efficacy of the formic acid treatment is still uncertain, histological preparations of known TSE brain and neural tissue should be regarded as potentially infective, and special care taken to avoid breaking the microscope slides or similar accidents during which penetrating injuries could occur. Once tissue blocks are fixed and acid-treated, sections can be cut on a standard microtome (using a disposable knife) and processed as usual. Debris (wax shavings) from section cutting should be contained and disposed of by incineration.

National and international transport of pathology specimens

4.43 Pathology specimens are subject to detailed national transport guidelines, directed towards ensuring that these goods are carried under optimum conditions for the safety of persons, property and environment. Carriage by rail or road in the UK is covered by the Classification, Packaging and Labelling of Dangerous Goods for Carriage by Road or Rail Regulations (1994). The transport of specimens from *known, suspect or at risk* patients should fulfil these requirements, and no other specific precautions need be taken.

4.44 The transportation of pathology samples, or deceased patients, by air from the UKneeds to comply with the International Air Transport Association (IATA) Restricted Articles Regulations, and any additional requirements of the individual carriers. Documentation required by the IATA includes a Shippers Certificate for Restricted Articles, which requires content, nature and quantity of infectious material to be disclosed.

Community Healthcare

4.45 When caring for *known, suspect or at risk* patients in the community, the principles outlined in the section on hospital care are equally applicable. Either in hospital or in community healthcare, standard infection control procedures will minimise the risk of infection transmission, not only to the care-givers, but also to members of the surrounding community and population in general.

4.46 Clinical waste generated as a result of community care-based treatment, e.g. swabs and sharps, should be handled as for any clinical waste, and be disposed of by incineration. Guidance on the handling of clinical waste has been published and a new edition is due in 1998 (see bibliography).

4.47 Spillages of body fluids or waste material should be handled as previously recommended (see paragraph 4.16).

4.48 Used or fouled bed linen (i.e. contaminated with body fluids or excreta) should be removed from the bed and washed and dried in accordance with convention (HSG 1995). Provided that care is taken, bed linen is unlikely to represent an infection risk; however to further reduce the risk, gloves should be worn and hands washed and dried after contact. No further handling or processing requirements are necessary.

4.49 In the event that a *known, suspect or at risk* patient becomes pregnant, no particular precautions need to be taken during the pregnancy other than normal ante-natal care. However, during and after the birth, particular precautions should be taken to reduce the risk of transmission (see paragraph 4.14). If a home delivery is decided upon, it is the responsibility of the midwife to ensure that any contaminated material is removed and disposed of in line with correct procedures for infected clinical waste.

4.50 Late stage CJD patients may well experience tissue breakdown and the development of extensive pressure point sores. These lesions should be dressed regularly, using standard infection control precautions, and contaminated dressings disposed of as clinical waste by incineration.

4.51 The British Dental Association (BDA) has issued general guidance on the development of practice infection control policies. Individual practice infection control policies, if developed and implemented efficiently, will minimise the risk of transmission of infection. Based on the advice in this document, the BDA are understood to be preparing specific advice for dental procedures on *known, suspect or at risk* patients.

After Death

4.52 On the death of a *known, suspect or at risk* patient, the removal of the body from the ward, community setting or hospice, to the mortuary, should be carried out using normal infection control measures. It is recommended that the deceased patient is placed in a body bag prior to transportation to the mortuary, in line with normal procedures for bodies where there is a known infection risk.

Post mortem

4.53 Currently *post mortem* examinations are essential in order to confirm the clinical diagnosis and the cause of death as CJD or a related disorder. However, such procedures have the potential to expose pathologists and mortuary staff to infectious materials. The following paragraphs give advice on basic precautions for safe working. Further advice is given in the Health Services Advisory Committee publication Safe working and the prevention of infection in the mortuary and *post mortem* room. Specific information on neuropathological autopsy in CDJ cases has been published (see bibliography).

4.54 Only fully trained staff should undertake any necessary *post mortem* examination on *known, suspect or at risk* patients. Ideally three people should be present during the examination: The pathologist assisted by one technician, and a further circulator to open or label specimen containers. Observers should be prohibited or kept to a minimum. *Post mortem* technicians, and others attending out of necessity, should be fully trained in or informed of procedures for such *post mortems* and made aware of the relevant history of the patient.

4.55 Restricted *post mortem* examinations on CJD cases can be undertaken in any mortuary. If only an examination of the brain is to be undertaken, the scalp is reflected in the normal way with absorbent wadding underneath the head to soak up CSF and other material when the cranium is opened. The head and neck of the cadaver should then be enclosed in a large polythene bag. The bag serves to contain bone dust while opening the cranium with either an electrical oscillating saw or hand saw. The bag and skull cap can be detached together before sampling the CSF and removing the brain and pituitary.

4.56 If a full scale *post mortem* examination of a case of CJD is indicated, including removal of the viscera and spinal cord, it is recommended that the body is removed for special handling in a high risk autopsy suite. Arrangements for refund of any removal costs for bodies for CJD autopsies are made through the CJD Surveillance Unit.[5] To minimise contamination of the working environment, *post mortem* examination should be carried out with the body in an open body bag with absorbent wadding. On completion of the autopsy, the body should be sewn up leaving the wadding *in situ* in the body bag. This has the advantage of absorbing fluids. Any excess wadding should be incinerated. Care should be taken in sewing up the body that burning through gloves does not occur by pulling too hard on the twine. The body bag is then sealed. In some circumstances, it may be necessary to remove the body from the bag for autopsy; in these cases the body should be placed into another bag after autopsy, using absorbent wadding as previously, and the original bag should be disposed of by incineration.

4.57 Disposable protective clothing should be worn including theatre suit, gown, apron, hat and double gloves, and a face visor, which completely encloses the operators head to protect the eyes, nose and mouth. Consideration should be given to the use of hand protection, such as armoured or cut-resistant gloves.

4.58 Disposable instruments should be used wherever possible, and incinerated after use. If this is not feasible, a set of dedicated instruments for *known, suspect or at risk* cases is recommended, in order to minimise the frequency of their use and the risk of transmitting infection. Manual or electric saws may be used, although the former do not create aerosols and are easier to decontaminate after use. Instruments and mortuary working surfaces should be decontaminated following the guidance in Annex B.

Anatomy and pathology teaching

4.59 Anatomy Departments are advised not to accept for teaching or research purposes bodies, brain or spinal cord from *known, suspect or at risk* patients. Departments should make enquiries of those responsible for donating the body, and of the medical staff who were involved in the care of the donor, whether any of the above apply to the donor. Such information will

also be useful when formulating their own guidance on exclusion criteria for prospective donors.

Undertakers and Embalmers

4.60 Concern about possible unknown CJD cases does not warrant a level of precaution for undertakers handling intact bodies other than those used generally for all work of this nature. In cases of traumatic injury, it is sensible general practice to minimise contact, particularly in circumstances under which penetrating injuries could arise. Cosmetic work on bodies of patients from a risk group may be undertaken, taking the precautions routinely used when dealing with human cadavers.

4.61 Where the diagnosis of CJD is *known or suspected* it is advisable to avoid embalming procedures.

Funerals and Cremations

4.62 Relatives of the deceased may wish to view or have some final contact with the body. Such viewing, and possible superficial contact, such as touching the face, need not be discouraged.

4.63 There have been some concerns expressed about whether burial or cremation presents any risks of environmental contamination. Although it is difficult to quantify the risk of environmental contamination associated with burial, due to the range of unknown factors, it is accepted that the risk is likely to be vanishingly small, and there is no need to discourage burial. Similarly, the risk of residual infectivity after cremation is likely to be negligible. There is no need for extra precautions to be taken for either burial or cremation.

4.64 There are no additional precautions needed for transporting the body within the UK. If there is a need to transport the body internationally, it will be necessary to comply with the IATA Restricted Articles Regulations, and any additional requirements of the individual carriers. It should be noted that the IATA Regulations do require embalming of the body.

Exhumations

4.65 A Home Office licence is required before an exhumation can take place. Those involved with such a procedure should follow normal standard practice for exhumations.

[5]Enquiries should be made to National Creutzfeldt-Jakob Disease Surveillance Unit, Neuropathology Laboratory, Western General Hospital, Crewe Road, Edinburgh EH4 2XU. Telephone 0131 537 1980.

Annex A
Distribution of TSE Infectivity in Tissues and Body Fluids

The following tables present current information on the distribution of TSE infectivity in tissues and body fluids based on data from experimental studies, where available, and on information from other studies of natural TSE disease in humans and animals. A knowledge of the likely distribution of infectivity in tissues is important in deriving risk assessments for experimental work with tissues potentially infected with TSEs. However, the risk assessments must be updated as further information becomes available. The following tables must only be used as a guide to assist in deriving local risk assessments, which need to take into account other factors such as the origin of the TSE agent.

Table A.1
Catagorisation of tissues based on infectivity titres in tissues and body fluids from naturally infected goats and Suffolk sheep with clinical Scrapie (see also Table A.2)

Category	High infectivity	Medium infectivity	Low infectivity	No detectable infectivity	
Sheep and goats		brain spinal cord	colon-proximal ileum-distal lymph nodes pituitary gland rectum-distal+ spleen tonsil	adrenal gland bone marrow** cerebrospinal fluid colon-distal liver** lung** nasal mucosa pancreas** sciatic nerve thymus**	blood clot faeces fetus heart kidney mammary gland milk muscle-skeletal ovary placentao saliva salivary gland seminal vesicle serum testis thyroid uterus

Based on data derived from Hadlow W. J. *et al*, 1980, 1982; and from tables produced by the World Health Organisation Consultations 12-14 November 1991 and 17-19 May 1995, and the European Commission 14-15 September 1993.
+ = not assayed but high content of lymphoreticular tissue ** = trace or exceptional
o = positive in other studies (Pattison et al 1972, 1974)

Table A.2
Infectivity in tissues based on other studies of natural disease

Other tissues in which infectivity is assumed or known as a result of other studies of natural disease include:	**Other tissues which have shown NO detectable infectivity in other studies of natural disease include:**

cornea	- iatrogenic CJD	CJD:
dura mater	- iatrogenic CJD	faeces, hair, saliva, skin, sweat, tears and
kidney	- kuru and CJD	urine
lung	- CJD	
pituitary gland	- iatrogenic CJD	Scrapie:
placenta	- scrapie, sheep	colostrum (in one pre-clinical sheep tested),
retina	- BSE	skin

BSE:
abomasum, buffy coat, distal colon, embryos, epididymis, fetal calf blood, fetal fluids, midrum fat, muscles with cranial or spinal nerve supply, oesophagus, optic nerves, prostate, proximal small intestine, reticulum, rumen omasum, semen, skin, splanchnic nerves, tibial nerves, trachea (cartilage), uterine caruncle (pregnant cow)

Annex B
Cleaning, Decontamination and Waste Disposal

General

1. The agent thought to be responsible for CJD is recognised as being particularly resistant to standard physical and chemical methods of inactivation and decontamination. The standard autoclave regimen of 121C for 15 minutes is ineffective, and autoclaving at 134C for 3 minutes cannot be relied upon for equipment decontamination. Gases such as ethylene oxide and formaldehyde are ineffective, as are some chemical disinfectants such as alcohols, formalin, aldehydes (such as glutaraldehyde), propiolactone, hydrogen peroxide, iodophors, peracetic acid and phenolics. Sodium hypochlorite has been shown to be effective but at concentrations that pose certain practical constraints. Sodium hydroxide has a substantial effect but is not completely inactivating. Ionising or UV irradiation at conventional doses and dry heat are also not effective. The effectiveness of other processes and agents such as gas plasma have yet to be fully evaluated. Table B.1 gives a summary of recommended processes and agents, and Table B.2 those shown to be ineffective.

2. As many of the standard methods of decontamination cannot ensure complete inactivation of the agent, the emphasis must be on removal of the agents by thorough cleaning. This should be followed by an appropriate autoclaving or liquid chemical treatment as described below. Table B.3 gives a summary of the basic precautions for decontamination.

3. It is important to note that the advice here for the decontamination of instruments refers only to instruments that have been used on at risk patients where there has not been involvement of the brain, spinal cord or eye. All instruments used on *known or suspect* patients, and those used on *at risk* patients where there has been exposure to brain, spinal cord or eye must be disposed of by incineration. For *suspect* patients quarantine procedures can be used to hold the instruments pending confirmation of the diagnosis (see paragraph 4.28 in the main text).

4. Manufacturers of CE-marked re-usable medical devices are required to supply information on the appropriate processes to allow re-use (Medical Devices Regulations, 1994 - see list of references at the end of this Annex). Users should consult this information to ensure that the instruments are able to withstand the required decontamination processes, which are more rigorous than the processes normally used for re-processing. If there is any doubt, the manufacturer of the instrument or equipment should be contacted for further advice.

Table B.1
Chemicals & process RECOMMENDED for use against TSE agents

Chemical disinfectants	Gaseous disinfectants	Physical processes
20,000ppm available chlorine of sodium hypochlorite for 1 hour	none	porous load steam steriliser 134-137oC for a single cycle of 18 minutes, or 6 successive cycles of 3 minutes each*.;
2M sodium hydroxide for 1 hour*		
For histological samples only, 96% formic acid for 1 hour		

* but known not to be completely effective.

Table B.2
Chemicals & process INEFFECTIVE against TSE agents

Chemical disinfectants	Gaseous disinfectants	Physical processes
alcohols	ethylene oxide	dry heat
ammonia	formaldehyde	
-propiolactone		
chlorine dioxide		ionising, UV or microwave
formalin		radiation
glutaraldehyde		
hydrochloric acid		moist heat at 121oC
hydrogen peroxide		for 15 minutes
iodophors		
peracetic acid		
phenolics		
sodium dichloroisocyanurate		
(e.g. Presept)**		
10,000ppm sodium hypochlorite		

** the rate of release of chlorine from this product is insufficient to ensure complete inactivation of the agent.

Table B.3
Basic precautions for disinfection and decontamination

- Clean instruments thoroughly at least twice to remove body fluids prior to disinfection.
- Use automated decontamination processes where possible, and avoid mixing routine instruments with those used in TSE-related work in the same cycle.
- Recycle durable items for re use only after appropriate decontamination use only stringent autoclaving procedures or recommended chemical disinfection methods.
- Where possible, cover surfaces with disposable material, which can then be removed and incinerated; otherwise clean and decontaminate surfaces thoroughly use only recommended decontamination procedures.
- Use absorbent material to soak up spillages, which can then be contained and incinerated.
- Use secure leak-proof containers, e.g. double bagging, for the safe handling of clinical waste.
- Avoid external contamination of the waste container.
- Wear protective clothing at all times.

Cleaning contaminated instruments

5. Manual handling of contaminated instruments should be kept to a minimum and automated decontamination processes, as described below, should be used wherever possible.

6. The cleaning of contaminated items to remove all body fluids and tissues in which a transmissible agent may be present is critical in ensuring the effectiveness of the decontamination regime. All items should be cleaned at least twice before treatment with moist heat or liquid chemicals. The first clean should be carried out in an ultrasonic cleaner; the second in an automated thermal washer/disinfector. Neutral or enzymatic detergent suitable for use with this processing equipment should be used.

7. Contaminated instruments should be processed through a covered ultrasonic bath and automated washer/disinfector in which no other instruments are being cleaned.

8. Items should be cleaned as soon as possible after use to minimise drying of blood and body fluids onto the item, which may then be more difficult to remove. Items should not be soaked in disinfectants prior to cleaning. Further details on the use of ultrasonic cleaners, thermal washer/disinfectors and manual cleaning are contained in the guidance from the Microbiology Advisory Committee on decontamination (see list of references at the end of this Annex).

9. Staff carrying out the cleaning and subsequent processing of instruments and equipment should follow standard basic precautions for avoiding exposure to infectious material (e.g. use protective clothing, cover abrasions with waterproof dressings, avoid use of sharps).

Decontaminating the cleaning equipment

10. Following processing of instruments, the ultrasonic bath and automated washer/disinfector should be run through an empty cycle. Any solid waste/tissue should be disposed of by incineration. Liquid waste should be disposed of safely, either by normal direct discharge from automated washers, or by collection and inactivation from equipment such as ultrasonic baths. Any cleaning aids such as brushes, if used, should be disposed of by incineration.

Autoclaving

11. After cleaning, the items should be processed in a porous load (high vacuum) steam sterilizer using one of the following cycles. **Downward or upward displacement autoclaves must not be used**:

- a single cycle of 134-137C for a minimum holding time of 18 minutes; or
- 6 successive cycles of 134-137C for a minimum holding time of 3 minutes for each cycle.

Other cycles are *not* recommended.

12. The sterilizer should have been validated and routinely tested in accordance with HTM 2010 (see list of references at the end of this Annex).

13. Whilst it has been suggested that the above cycles may not be entirely effective (Taylor *et al* 1994 - see list of references at the end of this Annex), it is considered that a substantial reduction in the level of contamination, i.e. the two-step process of cleaning to remove most of the body fluids or tissues in which the transmissible agent may be contained and protected, followed by processing through one of the above moist heat cycles, will be sufficient.

14. Recent work has suggested that a combination of autoclaving and chemical treatment may be effective (Taylor *et al* 1997 - see list of references at the end of this Annex). Further work is required to support this approach before it can be recommended.

Treatment of instruments with liquid chemicals

15. If the instrument is unable to tolerate the moist heat porous load cycles specified above, then liquid chemical treatment may be considered.

16. Chemical agents and contact times that have been found to be most effective include:

- 20,000ppm available chlorine of sodium hypochlorite for 1 hour;
- 2M sodium hydroxide for 1 hour.

Notes:

1. 10,000ppm hypochlorite must not be used as it is ineffective against the agents of TSE at this concentration.
2. Sodium dichloroisocyanurate (commonly used as 'Presept' tablets) has been shown also to be ineffective.

17. However, these chemical agents at the concentrations and contact times specified may have a detrimental effect on clinical instruments and equipment, and should only be used after seeking advice from the manufacturer of the instrument to ensure the item will withstand these corrosive processes (see paragraph 4 of this Annex).

Surface decontamination and the management of spillages

18. The above disinfectants should be used for cleaning surfaces. For the decontamination of surfaces, repeated wetting with the disinfectant is necessary over the treatment period. As this concentration of hypochlorite can be corrosive for some commonly used surface finishes, work that involves the handling of infected material should be conducted only on resistant surfaces or work benches shielded by disposable absorbent plastic-backed coverings. The use of enamel, heat-stable plastic or disposable trays is recommended to confine contamination. These should be autoclaved, and the disposable items incinerated after use.

19. For minor spillages, the surface should be disinfected as above. For spillages of larger volumes of liquid, absorbent material should be used to absorb the spillage (a number of proprietary absorbent granules are available for such use). The surface should be disinfected as above, and all waste disposed of as clinical waste by incineration. Disposable gloves and an apron should be worn when removing any spillage and these should be disposed of by incineration.

Inactivation of samples

20. All tissues for histological examination should be immersed in 96% formic acid for 1 hour after routine fixation, unless they have been exposed to phenol. If samples have been exposed to phenol it is not considered safe to then expose them to formic acid. Such samples should therefore be handled as un-decontaminated tissue.

21. Paraffin sections from blocks of tissue not previously decontaminated should be immersed in 96% formic acid for 5 minutes after de-waxing.

22. Clinical samples, e.g. CSF, should be autoclaved or immersed in a solution of sodium hypochlorite resulting in 20,000ppm free chlorine for 1 hour before final disposal by incineration.

Decontamination of safety cabinets

23. Formalin, or rather, in this context, gaseous formaldehyde, which is the conventional medium for the fumigation of safety cabinets, is not effective against TSE agents. Nonetheless, fumigation will need to be carried out as a precaution against other infectious agents that may be impacted on the surface of the cabinet's HEPA filter. The unit should be decontaminated before changing filters.

24. Due to the difficulties associated with their decontamination, it is recommended that safety cabinets used for work with TSE agents should be of the type with the facility for removing HEPA filter units by bagging. Whether or not bagging of the filter as it is withdrawn is possible, spraying the filter face after fumigation and before removal with 'eg hair spray' will help to limit the shedding of particulate matter. Where a Class II cabinet (BS:5762:1992) is to be used, a model that has the main HEPA

filter immediately below the work surface is preferred, as this will prevent contamination of the plenum of the cabinet. With the filter in this position, use may be made of liquid latex to seal the filter surface before removal. Pre filters (dust filters) are generally easily removed, and after immersion treatment with 2M sodium hydroxide solution (see above) to limit dust dispersal they should be contained securely for incineration or safe transport to the autoclave. If made of durable but not heat stable material, they may, alternatively, be treated with hypochlorite solution containing 20,000 ppm available chlorine.

25. Working in a shallow tray in the cabinet will limit dispersal onto work surfaces by splashing, but it is essential to ascertain, by testing the cabinet with the tray *in situ*, that containment for operator protection is not affected (see BS 5726:1992 for detail of containment testing). Another option is to tape disposable plastic-backed absorbent paper to the working surface in order to minimise contamination. The covering must be renewed regularly (preferably after each period of work) and incinerated.

Waste disposal

26. All material classified as clinical waste should be disposed of by incineration at an authorized incineration site. For the safe handling of clinical waste, use secure leak-proof containers, e.g. double bagging, where appropriate. Avoid external contamination of the container.

References in Annex B

1. Medical Devices Regulations 1994 (SI 1994 No 3017).
2. Department of Health. Sterilization, Disinfection and Cleaning of Medical Equipment: guidance on decontamination. Microbiology Advisory Committee to the Department of Health Medical Devices Agency, Part 1: Principles, Part 2: Procedures.
3. Department of Health (1994). HTM 2010 Part 3: Validation and verification: Sterilization. HMSO.
4. Taylor DM, Fraser H, McConnell I, Brown KL, Lamza KA and Smith GRA. (1994). Decontamination studies with the agents of bovine spongiform encephalopathy and scrapie. *Arch Virol* 139 313-326.
5. Taylor DM, Fernie K and McConnell I. (1997). Inactivation of the 22A strain of scrapie agent by autoclaving in sodium hydroxide. *Vet Microbiol* 58 87-91.

Bibliography

Advisory Committee on Dangerous Pathogens (1995). Categorization of biological agents according to hazard and categories of containment. HSE Books. ISBN 0-7176-1038-1.

Advisory Committee on Dangerous Pathogens (1998). Supplement to Categorisation of biological agents according to hazard and categories of containment. HSE Books. ISBN 0-7176-1038-1.

Advisory Committee on Dangerous Pathogens (1996). BSE (Bovine Spongiform Encephalopathy) Background and general occupational guidance. HSE Books. ISBN 0-7176-1212-0.

Advisory Committee on Dangerous Pathogens (1997). Working safely with research animals: management of infection risks. HSE Books. ISBN 0-7176-1377-1.

Advisory Committee on Dangerous Pathogens (1994). Guidance on precautions for work with human and animal transmissible spongiform encephalopathies. HMSO. ISBN 0-11-321805-2. Also notified under Department of Health professional letter, PL(94)CO/5.

British Dental Association (1996). Infection Control In Dentistry.

Bruce ME *et al*. (1997). Transmissions to mice indicate that new variant CJD is caused by the BSE agent. *Nature* **389** 498-501.

Department of Health and Social Security (1981 and 1984). The management of patients with spongiform encephalopathy (Creutzfeldt-Jakob Disease CJD). Circulars DA(81)22 and DA(84)16.

Department of Health (1992). Neuro and ophthalmic surgery procedures on patients with or suspected to have, or at risk of developing CJD or GSS. Professional letter, PL(92)CO/4.

Department of Health (1995). Hospital laundry arrangements for used and infected linen. Health Service Guidance, HSG(95)18.

Department of Health. Hospital Infection Working Group of the Department of Health and the Public Health Laboratory Service (1995). Hospital Infection Control: Guidance on the control of infection in hospitals. Health Service Guidance HSG(95)10.

Department of Health and Public Health Medicine Environmental Group Working Group (1996). Guidelines on the Control of Infection in Residential and Nursing Homes.

Health and Safety Executive (1996). Free leaflet on Consulting Employees On Health And Safety. A Guide To The Law. HSE Books. IND(G)232L. Health and Safety Executive (1996). Free leaflet on Occupational health risks from cattle. Agricultural Information Sheet number 19. HSE Books.

Health and Safety Commission (1994). Control of Substances Hazardous to Health Regulations 1994. Approved Codes of Practice. HSE Books. ISBN 0-7176-1308-9.

Health Services Advisory Committee (1997). Management of Health and Safety in the Health Services: Information for Directors and Managers. HSE Books. ISBN 0-7176-0844-1.

Health Services Advisory Committee (1992). Safe disposal of clinical waste. HSE Books. ISBN 0-7176-0447-0.

Health Services Advisory Committee (1991). Safe working and the prevention of infection in the mortuary and post-mortem room. HSE Books. ISBN 0-11-885448-8.

Hill AF *et al*. (1997). The same prion strain causes nvCJD and BSE. *Nature* **389** 448-450.

Ironside JW and Bell JE. (1996). The high-risk neuropathological autopsy in AIDS and Creutzfeldt-Jakob Disease: principles and practice. *Neuropathology and Applied Neurobiology* **22** 388-393.

Spongiform Encephalopathy Advisory Committee (1994). Transmissible Spongiform Encephalopathies: A Summary of Present Knowledge and Research. HMSO. ISBN0-11-242987-4

The priced publications are available directly from either:
The Stationery Office
PO Box 276
London SW8 5DT
Telephone orders: 0171 873 9090
General enquiries: 0171 873 0011
Fax orders: 0171 873 8200

or

HSE Books
PO Box 1999
Sudbury
Suffolk CO10 6FS
Telephone: 01787 881165
Fax: 01787 313995

and through good booksellers

Membership of working group

Members

Dr M J Crumpton	Chairman, the Advisory Committee on Dangerous Pathogens
Mr R Bradley	Central Veterinary Laboratory, New Haw, Surrey. Member of the SEAC.
Mr A R Clare	Confederation of British Industry. Member of the ACDP.
Dr J Ironside	National CJD Surveillance Unit, Western General Hospital, Edinburgh.
Prof. D Jeffries	Department of Virology, St Bartholomews Hospital, London. Member of the ACDP.
Dr P Jones	Institute for Animal Health, Compton, Berkshire. Member of ACDP.
Mrs T McGuire	Lothian NHS Occupational Health Service, Astley Ainslie Hospital, Edinburgh. Member of the ACDP.
Dr R Owen	Trades Union Congress. Member of the ACDP.
Dr M Painter	Infection Control and Surveillance Unit, Gateway House, Manchester. Member of the SEAC.
Prof. S Palmer	Communicable Disease Surveillance Centre, Welsh Unit, Roath, Cardiff.
Prof. P Smith	Department of epidemiology and population sciences, London School of Hygiene and Tropical Medicine, London. Member of the SEAC.
Dr D Taylor	Institute for Animal Health, Neuropathogenesis Unit, Edinburgh.
Dr T Wyatt	Department of Microbiology, Mater Hospital Trust, Belfast. Member of the ACDP.

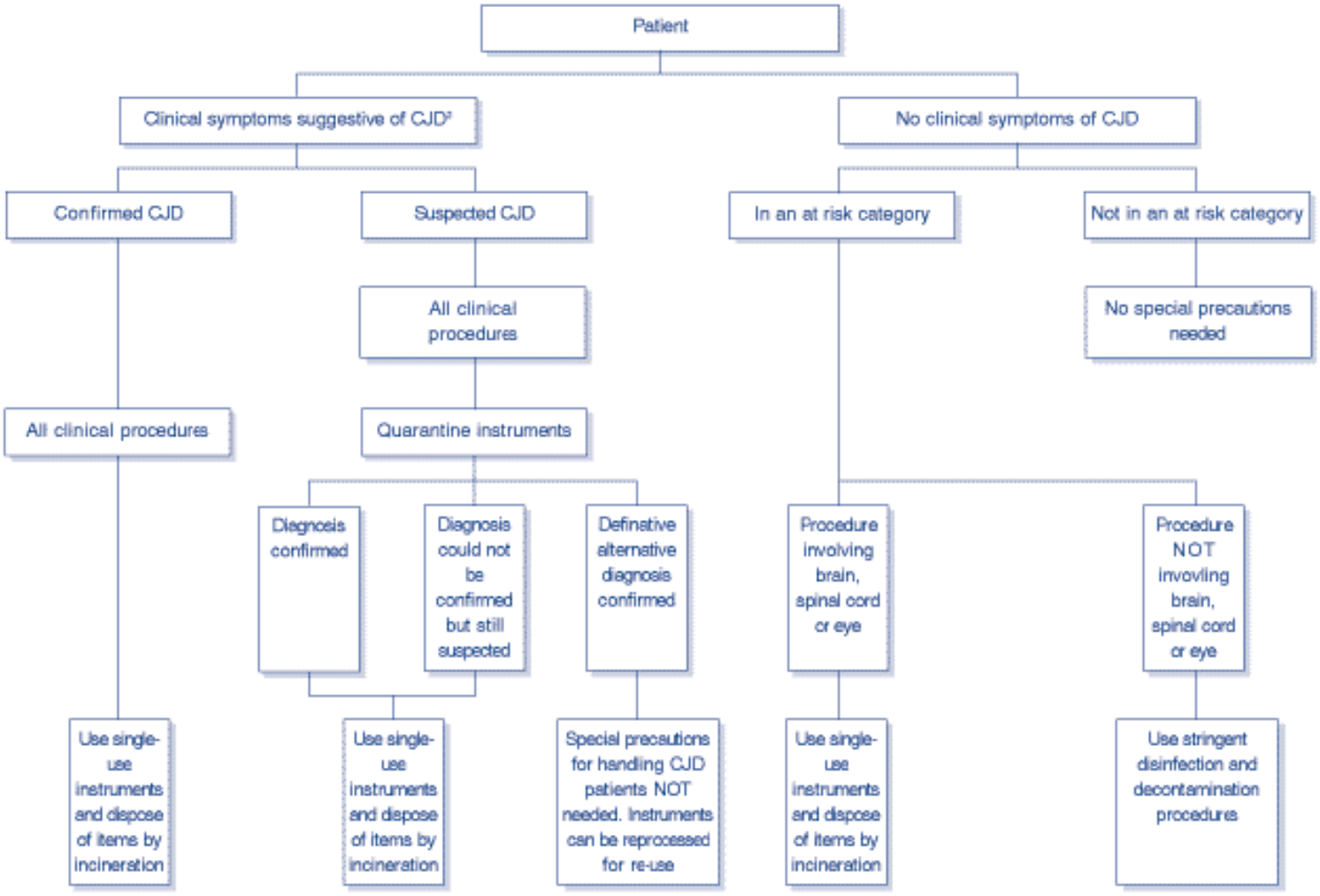
Officials

Dr D Matthews	Ministry of Agriculture Fisheries and Food
Mr I Strudely	Health and Safety Executive
Dr A Wight	Department of Health

Secretariat

Dr M Bale	Health and Safety Executive
Mrs A Harrington	Health and Safety Executive
Mrs E Lawrence	Department of Health
Dr A Nolan	Ministry of Agriculture, Fisheries and Food
Miss K Norman	Department of Health
Mr M Skinner	Department of Health

Algorithm chart for precautions for clinical procedures on known, suspect or at risk[1] patients



[1] as defined in Table 4 [2] includes classical sporadic CJD, nvCJD, GSS, FFI and kuru