Guidance

Minimise transmission risk of CJD and vCJD in healthcare settings

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Part of: Creutzfeldt-Jakob disease (CJD): guidance, data and analysis
Applies to: England

Prevention of CJD and vCJD by Advisory Committee on Dangerous Pathogens' Transmissible Spongiform Encephalopathy (ACDP TSE) Subgroup.

Documents

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PDF, 105KB, 10 pages

Health and safety management of transmissible spongiform encephalopathy
PDF, 34.5KB, 12 pages

Laboratory containment and control measures
PDF, 155KB, 22 pages

Infection control of CJD, vCJD and other human prion diseases in healthcare and community settings
PDF, 448KB, 23 pages

Annex A1: Distribution of transmissible spongiform encephalopathy infectivity in human tissues and body fluids
PDF, 227KB, 5 pages

Annex A2: Distribution of infectivity in animal tissue and body fluids
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Annex B: Diagnostic criteria
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Annex C: General principles of decontamination and waste disposal
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Annex L: Managing CJDvCJD risk in ophthalmology
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Annex M: Managing vCJD risk in general surgery and liver transplantation
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CJD guidance for ophthalmologists
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Information sheet for funeral directors, relatives and others following a CJD death
PDF, 17.2KB, 1 page

Alert to urological surgeons regarding the equipment used for patients at risk of vCJD requiring transrectal prostatic biopsy
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Frequently asked questions
PDF, 237KB, 5 pages

Abbreviations
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PDF, 109KB, 4 pages

Detail

This guidance produced by the Advisory Committee on Dangerous Pathogens' Transmissible Spongiform Encephalopathy (ACDP TSE) Risk Management Subgroup aims to help minimise the risk of transmission of CJD and vCJD in healthcare and other work settings.

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PART ONE

Background and Introduction

1.1. Transmissible spongiform encephalopathies (TSEs), otherwise known as prion diseases, are rare, fatal, degenerative diseases affecting the central nervous system (CNS), that occur in humans and certain other mammals.

1.2. There are several recognised TSEs, including Creutzfeldt-Jakob Disease (CJD) in humans, bovine spongiform encephalopathy (BSE) in cattle and scrapie in sheep. These and other TSEs 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[1,2,3]. A useful summary about these diseases has been published previously by the Spongiform Encephalopathy Advisory Committee (SEAC)[4]. Some of the important features relevant to occupational exposure are summarised below:

(a) TSEs are caused by unconventional infectious agents currently thought to be infectious proteins (apparently without nucleic acid) known as prions which do not share the normal properties of viruses or bacteria. The CNS contains the highest levels of infectivity which is associated with accumulation of a modified host-encoded protein, prion protein. In TSEs, prion protein undergoes a structural change (involving re-folding) to a conformer with an increased beta – sheet structure. This conformational change renders the abnormal prion protein more resistant to degradation, and is associated with infectivity. The abnormal form of prion protein is only found in TSEs, but the mechanism and site of its conversion are still uncertain.

(b) A common feature of all TSEs is the appearance of microscopic vacuoles in the grey matter of the CNS, giving a sponge-like appearance, from which the conditions derive their name. This change is accompanied by the accumulation of the abnormal form of the prion protein in the CNS.

(c) The commonest form of CJD occurs as a sporadic disease, the cause of which is unknown, although genetic factors (particularly the codon 129 polymorphism in the prion protein gene (*PRNP*)) influence disease susceptibility. The familial forms of human TSEs (see Box 1) appear to have a solely genetic origin and are closely associated with mutations or insertions in the *PRNP* gene. Most, but not all, of the familial forms of human TSEs have been transmitted experimentally to animals. There are no known familial or genetic TSEs of animals, although polymorphisms in the *PRNP* gene of some species (sheep for example) may influence the length of the incubation period and occurrence of disease.

(d) Although TSEs are not contagious, they are experimentally transmissible by inoculation and in some cases by oral challenge. Some animal TSEs, such as scrapie, are naturally transmissible to sheep and goats and chronic wasting disease (CWD) is naturally transmissible to several North American species of deer and elk, but how this is effected is still uncertain. Transmissible mink encephalopathy (TME) and BSE are feed-borne diseases. Transmission of TSEs to humans has occurred from both human and bovine sources, resulting in iatrogenic CJD and variant CJD respectively (see Box 1). Other animal TSEs, including scrapie, do not appear to cause human disease.

(e) TSE agents are not uniformly distributed in the tissues of affected individuals and infectivity levels vary at different stages of incubation. In general, during the clinical disease, CNS tissues (including the retina) pose the highest risk, lymphoid tissues, cornea and dura mater are lower risk and most body fluids and other tissues negligible risk (for more detail see Tables A1 and A2);

(f) 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 standard autoclaving (e.g. 134°C for 3 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;

(g) All TSEs are invariably progressive and fatal once clinical signs appear; there is currently no known effective treatment or prophylaxis, although this is an area of active research and clinical trials in humans have been established.

(h) 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.

1.3. The unconventional nature of the agent, together with the appearance of BSE in the mid-1980s and variant CJD 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

small and large laboratory animal accommodation as new information on these diseases continues to emerge. There is also 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 those causing TSEs, notably the Control of Substances Hazardous to Health Regulations 2002 (COSHH)[5]. These require employers to assess the risks in all cases where there may be exposure to biological agents and when appropriate introduce measures to either prevent or adequately control exposure. COSHH applies 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 laboratory work with TSE agents, materials and infected animals (i.e. where there is deliberate intention to work with the agent or where laboratory workers are handling material that may contain 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 control the risk of 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 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), pathology laboratory staff, post mortem technicians;
- funeral, cemetery and crematorium workers;
- local Consultants in Communicable Disease Control (CsCDC) and Health Protection Teams.

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 Advisory Committee on Dangerous Pathogens publication "BSE Background and general occupational guidance"[6]. Guidance on handling meat-and-bone-meal (MBM) material[7] and an information sheet on common zoonoses in cattle[8], 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 References.

Box 1 Human and Animal TSEs

The human TSEs occur in 3 groups:

- Idiopathic diseases: Sporadic CJD and sporadic fatal insomnia
- Familial diseases: Familial CJD, Gerstmann-Sträussler-Scheinker disease (GSS) and fatal familial insomnia
- Acquired diseases: Human agents: Kuru and iatrogenic CJD
  Bovine agent: Variant CJD

All human TSEs are very rare; the world-wide incidence of CJD is about 1 per million people each year. Sporadic CJD accounts for around 85% of all human TSEs; familial TSEs account for around 10-15% of cases and the remaining smaller numbers include the acquired human TSEs. In sporadic CJD the usual age of onset is late middle age (average age 65 years). Most patients present with rapidly progressive dementia with focal neurological signs including ataxia, myoclonus, visual disturbances and rigidity. Death usually occurs within 4-6 months of clinical onset. The clinical features of familial TSEs are much more variable, even within affected families. Some patients exhibit clinical features which resemble sporadic CJD, while in GSS most patients present with ataxia and other movement disorders before the onset of dementia. In sporadic and fatal familial insomnia, patients usually suffer from prominent sleep disturbances before the onset of other neurological abnormalities.

Kuru occurred as an epidemic in the Fore-speaking people in the Eastern highlands of Papua New Guinea and was first reported in 1957. Its transmission was associated with funeral rites involving ritual contact with, preparation of, and consumption of the entire body (including brains) of relatives who had died of kuru. The similarity, especially of the neuropathology, between kuru and scrapie, a disease of sheep that had been shown to be transmissible some 20 years earlier, led to the subsequent successful experimental transmission of kuru to primates. A link was thus established between human contact with kuru-infected tissues, their consumption and the eventual development of kuru. The incidence of kuru has been markedly reduced following the abolition of cannibalism coupled with health education, although recent cases still arise

from historical exposure, indicating a maximum (to date) incubation period of around 40 years. The shortest incubation period in kuru is reported to be about five years.

The first case of iatrogenic transmission of CJD was identified in 1974 in a corneal graft recipient. Since then several hundreds of cases of iatrogenic CJD have been reported, most of which have occurred in recipients of human-derived pituitary hormones or human-derived dura mater grafts. Other rarer sources of infection include contaminated neurosurgical instruments and intracerebral electrodes. Incubation periods for iatrogenic CJD range from 1-2 years for neurosurgical routes of transmission to over 30 years in some pituitary hormone recipients. World Health Organisation guidelines on TSE's in relation to biological and pharmaceutical products have been published recently[9].

In 1996, the National CJD Surveillance Unit in the UK[10,11] identified a new form of CJD, which is now known as variant CJD. Variant CJD generally affects young adults (mean age at onset 28 years) with a clinical illness that lasts on average for 14 months. The initial features include psychiatric abnormalities and sensory abnormalities, which are usually followed by ataxia, myoclonus and other movement disorders and accompanied by dementia. At the time of writing, over 140 cases of variant CJD have been identified, over 90% of which have been in the UK. Considerable uncertainty exists over the likely future numbers of variant CJD cases in the UK; there has been a small but important decline in the incidence of the disease in 2002. There is a substantial body of evidence from multiple transmission studies to indicate that the agent responsible for variant CJD is biologically indistinguishable from the BSE agent, making this the only known human TSE which has arisen from infection from another species.

There have been no confirmed cases of transmission of TSE by virtue of occupation. There have been a small number of reports of sporadic CJD in healthcare workers (including a neurosurgeon, retired laboratory workers and a pathologist) but their link with their occupation is speculative. There is no evidence at present that occupational exposure to BSE is a risk factor for variant CJD.

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 and elk species;
- feline spongiform encephalopathy (FSE) in domestic cats and captive exotic felines;
- spongiform encephalopathy in captive exotic ungulates.
- Spongiform encephalopathy reported in primates in a French zoological collection.

BSE was first confirmed in the United Kingdom in 1986. Up to December 2002 about 183,000 native-born cattle in the UK are known to have been affected, and a total of over 3,000 native-born cattle in several other countries, including most countries of the EU. Current statistics can be found on the Defra webiste[12]. A few cases have occurred in these and some other countries following export of live cattle from countries with BSE.

Affected animals become unsteady on their feet, lose weight and become nervous, hence the term 'mad cow disease'. The BSE epidemic has been in continuous decline since 1992/3 in the UK as a result of successive bans on feeding ruminant-derived protein and subsequently mammalian-meat-and-bone-meal to ruminants. All animals suspected of having BSE are compulsorily slaughtered and completely destroyed. Ruminant or more extensive feed bans are now applied throughout the EU and in many other countries of the world, even those unaffected by BSE.

Scrapie occurs in sheep, and more rarely in 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.

TME was first recognised in farmed mink in 1947 and has occurred sporadically since then, but there have been no reports since the 1990s. CWD in Rocky Mountain elk, mule deer and some other deer species is also a TSE. Originally seen only in wild-life facilities in the USA, CWD is now reported in free-ranging and farmed deer and elk in the USA and in Canada. There have been recent reports of CWD in elk exported from Canada to Korea. CWD has not been reported in Europe and TME has not been reported in the UK. TSEs have been recognised in domestic cats and captive, exotic felines and ungulates, most, but not all of which were born in the UK. Strain typing studies have indicated that at least some of these cases and perhaps all are due to exposure to the BSE agent, presumably by the dietary route. These 'mini-epidemics' appear to have subsided to obscurity as a result of the various bans to protect animal species from feed exposure to TSE agents.

Report of a spongiform encephalopathy in primate species in France, and a captive golden cat from Europe that died in Australia, did not involve any residence in the UK.

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PART 2

Health and Safety Management of TSEs

HEALTH AND SAFETY LEGISLATION

The key requirements of the health and safety legislation, which is appropriate for work with TSEs, are given in Table 2a below.

Table 2a

Health and Safety at Work etc Act 1974 requires: • employers and self-employed workers to ensure they provide and maintain workplaces, equipment and systems of work that are, so far as is reasonably practicable, safe to workers and the public; • employees to take care of their own and others' health and safety, and to co-operate with their employer or any other person to enable them to comply with health and safety duties; • *A guide to the Health and Safety at Work etc Act 1974 (L1)* gives further information.	**Management of Health and Safety at Work Regulations (MHSWR) 1999** require employers and self-employed workers to: • identify the measures they need to take by carrying out risk assessments; • institute safety management systems; • appoint persons to assist in health and safety management; • ensure co-ordination and co-operation where two or more employers or self-employer persons share a workplace; • make emergency arrangements; • provide information and relevant training for employees; • *Successful health and safety management (HSG 65)* gives further information.
Control of Substances Hazardous to Health (COSHH) Regulations 2002 provide a framework of actions designed to control the risk from a range of hazardous substances including biological agents. These actions include: • assess the risk; • prevent the risk by substitution if possible; • control the risks using appropriate measures *e.g. work process, systems and engineering controls;* • control exposure at source *e.g. adequate ventilation systems and appropriate organisational measures;* • control the working environment including general ventilation; • maintain, examine and test control measures; • provide suitable personal protective equipment (PPE) when adequate control of exposure cannot be achieved by other means; • monitor exposure at the workplace; • provide information, instruction and training for workers; • make arrangements for health surveillance of workers where necessary; • *COSHH: a brief guide to the regulations (INDG131 rev1);* *Control of Substances Hazardous to Health (Fourth edition). The Control of Substances Hazardous to Health Regulations 2002. Approved Code of Practice and Guidance (L5);*	**Genetically Modified Organisms (Contained Use) Regulations 2000 and Genetically Modified Organisms (Contained Use) (Amendment) Regulations 2002** require employers and self-employed workers to: • make a risk assessment for genetically modified micro-organisms in relation to human health and environmental protection and for genetically modified animals in relation to human health; • apply appropriate containment and control; • notify the Competent Authority to the Regulations of all premises being used for genetic modification; • notify the Competent Authority of certain activities; • *A guide to the Genetically Modified Organisms (Contained Use) Regulations 2000,* and *Contained use of genetically modified organisms (INDG86 rev2)* give further information.

Health Surveillance under COSHH: guidance for employers; *The management, design and operation of microbiological containment laboratories*; and *5 steps to risk assessment (INDG163 rev1)* give further information.	
Reporting of Injuries, Diseases and Dangerous Occurrences Regulations (RIDDOR) 1995 require employers and the self-employed to: • report any infection reliably attributable to work with live or dead humans or animals, exposure to blood or fluids or any potentially infected material derived from any of the above; • report any accident or incident that could result in the release of a TSE agent (or any other biological agent categorised in Hazard Group 3 or 4). *e.g.* percutaneous exposure to known infected brain material; • *Guide to the reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995* gives further information.	**The Carriage of Dangerous Goods (Classification, Packaging and Labelling) Regulations 1996** require consigners to: • classify the biological agent or substance containing the biological agent for transport according to the criteria laid down in the 'Approved Requirements' • determine the packing group and package in accordance with the appropriate packing instruction; • appoint a Dangerous Goods Safety Adviser if necessary; • *Are you involved in the carriage of dangerous goods by road or rail?*; *Approved Carriage List: Information approved for the carriage of dangerous goods by road and rail other than explosives and radioactive material (ACL)*; *European Agreement concerning the international carriage of dangerous goods by road (ADR)*; *Approved Vehicle Requirements. Carriage of Dangerous Goods by Road Regulations 1996 (AVR)*; and *Regulations Concerning the International Carriage of Dangerous Goods by Rail (RID)* give further information.

Health and Safety Management of TSEs

2.1 The ACDP publication '*The management, design and operation of microbiological containment laboratories*' provides guidance on the management of biological agents including TSEs, in the laboratory environment. The document sets out the standards for Containment Level (CL) 2 and 3 microbiological laboratories and should be read in conjunction with this guidance.

Health and Safety Law

2.2 Employers have duties under health and safety legislation to protect employees and non-employees from risks to their health and safety arising from work activities; non-employees include students and visitors.

2.3 A summary of the principal legal requirements relevant to work with TSEs is given in Table 2a.

2.4 Biological agents, as defined in the Control of Substances Hazardous to Health (COSHH) Regulations, include the agents that cause transmissible spongiform encephalopathies (TSEs). COSHH applies both to deliberate work with TSEs (*e.g.* in a laboratory) and to incidental exposure, as may occur in, for example, health care workers, farm workers and abattoir workers. COSHH outlines the requirements that apply for work with biological agents. General duties, which are relevant to all hazardous substances, including biological agents and chemicals, can be found in the main Regulations. Additional requirements relating to just biological agents are outlined in Schedule 3 of COSHH.

2.5 A risk assessment should be made for both these types of work. Reducing and controlling the risk for incidental exposure may be more reliant on safe systems of work and the use of PPE rather than the use of containment, although preventing or controlling exposure by this means should be considered in the first instance (as set out in the hierarchical approach required by COSHH). Guidance on managing and controlling both deliberate exposure and incidental exposure for health care workers is given in later sections of this document. Guidance on incidental exposure for farm and abattoir workers involved in the slaughter and processing of cattle can be found in the general guidance document '*BSE (Bovine spongiform encephalopathy): Background and general occupational guidance'* and in the supplement '*Guidance for handling meat and bone meal material*'.

Legal classification of biological agents

2.6 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 established 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 (2000/54/EC). Details can be found in the ACDP publication "Categorisation of biological agents according to hazard and categories of containment" and the 2000 supplement *[currently under review]*.

2.7 Classification of a biological agent is based on the risk of infection to a healthy worker using well-established criteria. 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 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. TSE agents, excluding scrapie and others not linked to BSE, are classified as Hazard Group (HG) 3 on the basis of these criteria. Part 3 of this document on laboratory containment and control measures provides further detail on classification of TSE agents.

General Principles of Control

2.8 For laboratories and animal rooms the appropriate containment level is derived from the hazard classification of the agent, or from what is suspected about the possible presence of an agent. COSHH requires that when working with an agent in a particular hazard group, the containment level selected should match the hazard group

of the agent. TSEs should normally be worked on in CL3 because they are classified as HG3 agents. (See paragraph 2.13 for advice about changing containment measures). Detailed guidance on control and containment measures in laboratories and animal rooms is given in Part 3 of this document.

2.9 When patients infected with a TSE agent are to be accommodated, for example on a hospital ward, the choice of controls and containment, as in other cases, should be on the basis of risk assessment. The level of risk should be the prime consideration. The controls selected should reflect the requirements outlined in COSHH with appropriate measures selected from Part II of Schedule 3 of COSHH. Detailed guidance on control and containment measures for TSE-infected humans is given in Part 4 of this document.

Risk Assessment

2.10 The Management of Health and Safety at Work Regulations (MHSWR) require all employers and self-employed people to assess the risks to their employees and others who may be affected by their work activity. More specifically COSHH requires assessment of the risks of work with substances hazardous to health. Where an assessment is carried out for the purposes of COSHH, or other more specific legislation, it does not have to be repeated for the purpose of MHSWR because the duties laid down in COSHH go beyond those in MHSWR and the more stringent requirements must be met. The risk assessment required by COSHH 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. It must include a review of all working procedures. For example, a 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.

2.11 The COSHH risk assessment for TSEs should consider:

- whether there is a deliberate intention to work with the agent, or if any exposure would be incidental to the work;
- the hazard group of the agent (see paragraph 2.7 above);
- the origin of the agent;
- the type of tissue handled (this will give an indication of the likely level of infectivity) (see Annex A);
- knowledge of expression of the agent in any experimental model and whether the work is likely to result in a high titre of infectivity;
- assessment of the type of task (*e.g.* concentration/propagation/purification); and
- the frequency of contact with the agents or materials likely to contain them;

- the possible routes of exposure including the potential for inoculation injury.

2.12 The local risk assessment for work involving propagation and concentration should be authorised by senior management.

Changing Containment Measures

2.13 All TSE agents should normally be worked on in Containment Level (CL) 3 conditions because they are HG3 agents. Scrapie, however, is not allocated to a hazard group as there is, to date, no evidence of transmission of disease to humans. Recent concern about BSE transmission from sheep has led to a debate on whether all scrapie strains should be handled at CL3. As this debate is ongoing, a precautionary approach should be adopted in which well characterised laboratory strains of scrapie should continue to be worked on at CL2, but extra precautions may be necessary for handling unidentified field isolates.

2.14 In some circumstances consideration may be given to changing the containment measures to reflect the likely exposure of workers to TSE agents in a particular circumstance. **Any decision to change the containment conditions should only be taken on the basis of a local risk assessment that takes into account:**

- **the type of work;**
- **the quantity of material;**
- **the likely infectivity to humans; and**
- **the procedures and equipment that will be used to propagate, concentrate or analyse the agent.**

2.15 Detailed guidance on the type of changes that could be made to the containment level is given in Part 3. If you are in any doubt about the basis for making changes to the containment measures you should consult HSE.

Local Safety Policies and Codes of Practice

2.16 The local health and safety policy sets out in general terms how management intend to develop and maintain a safe working environment. It should reference the ways in which the safe day-to-day working of the laboratory will be achieved and managed.

2.17 Specific information on the arrangements for working safely day-to-day can best be set out in local codes of practice. A guide to the main areas that should be covered is given in Infobox 1 below.

2.18 All employees must 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. Local codes of practice form part of this process of giving information on safe working, but thorough training and instruction on their day-to-day application is needed in order to make them work effectively. 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.

2.19 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' (INDG232L).

INFOBOX 1. TOPICS TO BE COVERED IN A LOCAL CODE

- **Introduction:**
  state the reasons for having a code;
  refer to other relevant health and safety documents;
  detail the arrangements for making staff aware of the nature of the TSE agent to which they might be exposed, the possible source of infection and the containment (physical and procedural) measures to be used; and
  training and supervision arrangements for working in the laboratory.

- **General Procedures:**
  specify which staff (or grade of staff) are authorised to carry out particular procedures; and
  provide appropriate guidance for ancillary and maintenance staff, contractors and visitors.

- **Operation of Unit**
  detail start up procedures, operation of safety cabinet, ventilation controls, procedures for operating equipment, use of personal protective equipment and cleaning procedures.

- **Local Rules**
  these should cover the circumstances in which changed containment measures may be used, eg automated analysis of low risk specimens.

- **Waste**
  detail waste disposal policy and disinfection policy including cleaning of fragile laboratory equipment, eg automated analyser, and what to do in the event of spillage.

- **Staff Health**
  arrangements for reporting and recording incidents, including the name of the person to whom incidents should be reported.

- **Testing and Maintenance**
  arrangements for the maintenance and testing procedures on engineering controls to be carried out.

- **Emergency Procedures**
  procedures for dealing with accidents involving TSE agents including the name of the person to whom accidents should be reported.

List of workers exposed to TSE agents

2.20 Under certain circumstances COSHH requires employers to keep a list of employees who are exposed to HG3 or 4 agents. **The decision to keep a list depends on the local risk assessment.** For TSE agents a list is only required where employees deliberately work with the agent. For example:

- those involved in laboratory research work and veterinary clinical work with a TSE agent;
- staff performing invasive clinical procedures on patients suspected to be suffering from CJD of any type, particularly where there is a risk of exposure to central nervous tissue, eye tissue or other tissues known to contain CJD infectivity (see table on infectivity of tissues in Annex A1);
- laboratory staff handling tissue specimens from patients with CJD of any type, in either routine or specialist neuropathology laboratories; or
- staff undertaking post-mortem examinations of patients who have died of CJD of any type or where CJD of any type is suspected.

2.21 The routine clinical care of patients with CJD or a related disorder is unlikely to pose a significant risk of exposure to CJD of any type and staff working with such patients would not need to be included on such a list.

2.22 In cases of unintentional exposure, a list may be required if the risk assessment shows that there is a significant risk. The risk is deemed to be significant if more than basic hygiene measures are necessary to protect staff or if the control measures listed in COSHH are specifically applied. The list should be kept where there is a likelihood of exposure and not simply when there has been a known incident or accident, although it should also include details of these. Recording details of incidents or accidents on this list is not the same as the requirement to report certain diseases and accidents to HSE under the Reporting of Injuries, Diseases and Dangerous Occurrences Regulations (RIDDOR).

2.23 The information that should be recorded includes the type of work done and, where known, any specific exposure, accident or incident. Because of the long latency period of TSE agents and their serious long-term sequelae, the list must be kept for 40 years after the last known exposure. This list is in addition to the health record (which is required for the purposes of health surveillance under COSHH or MHSWR) and must be made available to any doctor appointed to carry out health surveillance, *e.g.* the occupational health physician. It must also be available to any employee who is specifically responsible for health and safety.

2.24 Each employee recorded on the list must have access to the information that relates to him or her personally. The list may be kept with the individual's occupational health record. Data protection requirements will apply to the information being held; see Infobox 2.

INFOBOX 2: THE DATA PROTECTION ACT 1998

The requirements of the Data Protection Act 1998 may apply to any records (computerised or manual) kept about individuals (such as employees) in connection with health and safety legislation, eg health surveillance records. These requirements may include informing people that certain information is held on them and granting them access to that information, should they request it. Guidance on the Act can be requested from the Office of the Data Protection Commissioner, Wycliffe house, Water lane, Wilmslow, Cheshire SK9 5AF (Tel. 01625 545745) or by e-mail at data@dataprotection.gov.uk. (See the website at www.dataprotection.gov.uk for more information.)

RIDDOR

2.25 RIDDOR requires some accidents and exposures to be notified to HSE. These include 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. Accidents or incidents, which result in or could result in the release or escape of a TSE agent, must also be reported under RIDDOR as a dangerous occurrence.

Health Surveillance

2.26 Where appropriate both MHSWR and COSHH Regulations require employees to be under suitable health surveillance. Under MHSWR health surveillance must be provided, as appropriate, with regard to the risks identified by the risk assessment. Under COSHH, 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; or
- there are valid techniques for detecting indications of the disease or effect.

2.27 There are no valid techniques for detecting early indications of TSE disease at the present time. Health surveillance is therefore limited to setting up and maintaining individual health records for employees likely to be exposed to TSE agents. However, employers must remain aware to any new techniques that become available and adopt them as appropriate.

2.28 The health record is supplementary to the list of workers exposed to TSE agents (see paragraph 2.23). The minimum information that should be recorded is:

- personal details of the individual including full name (and maiden name for women if appropriate), date of birth, gender, permanent address and post code, national insurance number and the date when the present employment started;
- the type of work the employee does;
- records of accidents and incidents involving exposure to the TSE agent; and
- a historical record of jobs in the present employment which involve exposure to infectious or potentially infectious TSE material.

2.29 Further information on health surveillance can be found in Regulation 11(3) of the COSHH Approved Code of Practice.

References for Part 2

Legislation:

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Management of Health and Safety at Work Regulations (MHSWR) 1999.
SI1999/3242. The Stationary Office 1999. ISBN 0 11 0856252 2

Control of Substances Hazardous to Health (COSHH) Regulations 2002. SI2002/2677
The Stationary Office 2002. ISBN 0 11 042919 2

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SI2002/63 The Stationary Office 2002. ISBN 0 11 039273 6

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1995. SI1995/3163. The Stationary Office 1995. ISBN 01 1053 7523

The Carriage of Dangerous Goods (Classification, Packaging and Labelling)
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Guidance:

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Successful health and safety management (HSG 65) 2nd ed.
HSE Books 1997. ISBN 0 7176 2034 4 (A priced publication)

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Guide to the reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995 (L73)
HSE Books 1998. ISBN 0 7176 1012 8

Are you involved in the carriage of dangerous goods by road or rail? (INDG234)
HSE Books 2000. ISBN 0 7176 1676 2 (A free leaflet)

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HSE Books (Third ed) ISBN 0 7176 1681 9 (A priced publication)

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The Stationary Office. ISBN 0 11 941712 X

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HSE Books (Second ed) ISBN 0 7176 1680 0

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The Stationary Office 1998. ISBN 0 11 552032 5

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Supplement to “BSE (Bovine Spongiform Encephalopathy): Background and general occupational guidance” Guidance for handling meat and bone meal material.
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Categorisation of biological agents according to hazard and categories of containment (Fourth ed) 1995.

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Part 3

LABORATORY CONTAINMENT AND CONTROL MEASURES

Introduction

3.1 This section gives advice on safe working practices to help prevent the transmission of TSE agents during laboratory work with such agents or material that contains or may contain them. It covers:

- all experimental work with preparations derived from body fluids, including work with abnormal purified prion proteins or tissues known or likely to contain either human or animal TSE agents;
- all diagnostic laboratory work with preparations derived from body fluids or tissues known or likely to contain human or animal TSE agents – this includes work with animal tissues derived in the field for onward supply to laboratories for investigation where appropriate, for example, tissues derived for surveillance purposes; and
- research work with infected animals.

3.2 Guidance on work with any hosts or vectors in which TSE agents have been cloned using genetic modification and where expression may be achieved is given in the Advisory Committee on Genetic Modification's Compendium of Guidance (www.hse.gov.uk/hthdir/noframes/acgmcomp/acgmcomp.htm).

Formal classification of TSE agents

3.3 The causative agents of the following diseases are all classified as Hazard Group (HG) 3 agents as listed in the Health and Safety Commission's Approved List of Biological Agents (http://www.hse.gov.uk/hthdir/noframes/agent1.pdf)**.**

- Creutzfeldt-Jakob disease (CJD) including variant CJD (vCJD);
- Gerstmann-Sträussler-Scheinker Syndrome (GSS);
- Kuru;
- Fatal Familial Insomnia (FFI);
- Bovine Spongiform Encephalopathy (BSE) and similar diseases, including feline spongiform encephalopathy (FSE), spongiform encephalopathy (SE) in captive exotic ungulates, transmissible mink encephalopathy (TME) and chronic wasting disease (CWD). BSE experimentally transmitted to other species is also included.

3.4 The appropriate containment level for an agent is derived from the hazard grouping of the agent. When working with an agent (e.g. propagation or concentration) in a particular hazard group, the Control of Substances Hazardous to Health (COSHH) Regulations 2002 require that the containment level selected must match the hazard group of the agent as a minimum. Although TSE agents are formally classified as HG3 (see paragraph 3.3), the containment measures required when working with them may not necessarily fully meet Containment Level 3 (CL3) because of the agent's unique features (paragraphs 3.6-3.10).

The hazard group of the TSE agent forms the basis of a risk assessment to determine the appropriate containment and control measures.

3.5 Based on the current Hazard Grouping of TSE agents, the recommended overall Containment Levels are given in Table 3a below. Work is categorised according to the type of infectious agent and, for work with animals, the species being infected. Work with human TSE agents includes primary sources and any sub-passages of human derived agents in other species. Work with any animal TSE agent passaged in primates or in genetically modified mice with the human PrP gene should also be considered.

Infobox 1: Categorisation of work with scrapie

The causative agent of scrapie (and other TSE agents known not to be linked to BSE) is not listed in the Approved List of Biological Agents because there is no evidence of transmission of disease to humans to date. However, as a precaution, work with well characterised laboratory strains of scrapie should be carried out at CL2.

Recent concern about BSE transmission from sheep has led to a debate on whether all scrapie strains should be handled at CL3. As this debate is ongoing, a precautionary approach should be adopted where extra precautions, above those normally required at CL2, may be necessary for handling unidentified field isolates.

Table 3a

Containment Levels recommended for work with TSE agents

Laboratory work with:	**Overall Laboratory Containment Level**	**Animal Containment Level**
Human TSE Agents BSE and agents from animals with related TSE (FSE, SE in captive, wild bovines and felines) or any sub-passaged agents from these in any species TME and CWD	3	3 – small animals 1* – large animals
Scrapie agents	2	2 - small animals 1* - large animals
* ACL1 applies to housing of animals only, additional precautions will be required when working with such animals – see paragraphs 3.30 to 3.47		

3.6 As well as the properties of the agent affecting the containment measures used, there may be other circumstances where consideration may be given to changing the containment measures to reflect the likely exposure of workers to TSE agents. InfoBox 2 gives one example of a situation (processing samples from a surveillance scheme) when this approach has been taken. **However, any decision to change the containment conditions should only be taken after performing a local risk assessment (see COSHH ACoP and Guidance, in particular Schedule 3 and Appendix 2) that takes into account**:

- the nature of the work;
- the quantity and type of material being handled; and
- the procedures and equipment that will be used – consider the potential for dispersal of the agent, for contamination of workers, equipment or surfaces at all stages of the activity including handling, processing and disposal, and for contamination during the setting up, servicing and maintenance of the equipment.

3.7 Having completed the risk assessment, local rules/standard operating procedures should then be prepared detailing safe working practices. Specific guidance on the situations where containment measures can be changed is given in the following sections.

3.8 Although in many respects the requirements of a CL3 laboratory are outwardly similar to CL2 laboratories, because of the more hazardous nature of the agents the standards that must be achieved are higher. The key differences between CL3 and CL2 laboratories relate to the way in which they are managed, the need for special training, and the degree of supervision, in addition to the physical requirements of the laboratory itself. In terms of work with TSE agents, managers should ensure that:

- staff are competent and trained to carry out the work;
- they have received suitable information, instruction and training about risks; and
- there is appropriate supervision of the work in question.

3.9 Guidance on these aspects of laboratory management is given in the '*Management, design and operation of microbiological containment laboratories*'.

3.10 It should be noted that changing some of the physical containment measures does not imply that the work can be carried out at CL2. But, subject to following the guidance set out in the subsequent sections, a CL2 laboratory may be appropriate for certain types of work (see paragraphs 3.27 and 3.28).

Infobox 2: Changing the containment level

In some circumstances the risk of a HG3 agent being present in a sample is extremely low.

For example, the appropriate containment measure for work with tissues derived for

surveillance purposes will depend on what is known about the incidence of infection in the population that is being studied, and as a result the risk assessment may show that Containment Level (CL) 2 is appropriate for work with the tissues.

For example, some of the Defra data from their current surveillance scheme indicate a low incidence of positives for BSE:

In 'high risk' cattle

	Fallen stock (OTM)		Casualties (OTM)	
	%	Actual	%	Actual
2001	0.35	86/24660	0.59	231/39487
2002	0.16	118/73055	0.34	380/111633

Healthy cattle submitted to OTMS

	%	Actual
2001	0.001	1/14320
2002	0.008	12/142887

Casualties on arrival at abattoir (2002)

	%	Actual
Over 30 months old	0.12	3/2474
24-30 months old	0	0/961

(Matthews D, 2003, Pers. comm.)

Using these data the VLA risk assessment indicated that samples from these cattle could be worked at initially at CL2, due to the low risk of exposure.

GENERAL APPROACH TO SAFE WORKING PRACTICES APPLICABLE TO ALL LABORATORY WORK WITH TSE AGENTS

3.11 This general approach applies to all laboratory work whether human or animal diagnostics and to research work.

3.12 '*The management, design and operation of microbiological containment laboratories*' provides guidance on the management of biological agents including TSE agents, in the laboratory environment. The guidance sets out the standards for CL2 and CL3 microbiological laboratories, and it should be read in conjunction with this guidance

which sets out the specific and/or additional requirements for work with TSE agents. The ACDP guidance *'Working safely with research animals: Management of infection risks'* should also be read in conjunction with this guidance. The essential features of CL2 and CL3, as required by COSHH, are shown in Table 3b below.

Table 3b: Containment measures for CL2 and CL3 laboratories

Containment measure	Containment level	
	2	3
Air handling		
The work place is to be maintained at an air pressure negative to atmosphere	No	Yes
Input and extract air to the workplace are to be filtered using high efficiency particulate absorption (HEPA) or equivalent	No	Yes, on extract air
Security and access		
Access is to be restricted to authorised people only	Yes	Yes
The workplace is to be separated from any other activities in the same building	No	Yes
Efficient vector control, e.g. rodents and insects	Yes, for animal containment	Yes, for animal containment
An observation window, or alternative, is to be present so that occupants can be seen	No	Yes
Safe storage of biological agents	Yes	Yes
A laboratory is to contain its own equipment	No	Yes, as far as is reasonably practicable
Disinfection and disposal procedures		
The workplace is to be sealable to permit disinfection	No	Yes
Specified disinfection procedures	Yes	Yes
Surfaces impervious to water and easy to clean	Yes, for bench	Yes, for bench and floor (and for walls for animal containment)
Surfaces resistant to acids, alkalis, solvents and disinfectants	Yes, for bench	Yes, for bench and floor (and for walls for animal containment)
Incinerator for disposal of animal carcasses	Accessible	Accessible
Protective equipment and procedures		
Infected material, including any animal, is to be handled in a safety cabinet, isolator or other suitable containment	Yes, where aerosol produced	Yes, where aerosol produced

General protective measures

3.13 General, basic protective measures should be used wherever there is a risk of exposure to potentially infectious material, including TSE agents. These measures are summarised in Table 3c in the context of working with TSE agents.

Table 3c General protective measures

- apply general good hygiene measures such as not eating, drinking, smoking or taking medication in the laboratory
- protect skin wounds such as cuts, abrasions, eczematous lesions with water proof dressings
- wear the appropriate protective clothing routinely – consider the use of disposable gowns and wear disposable gloves for all work with TSE material
- wear eye protection or full face visor to protect eyes and mucous membranes from splashes with potentially infected material
- minimise the use of sharps (needles, knives, scissors and laboratory glassware) wherever possible
- consider the use of suitable hand protection such as armoured glove(s) where the use of sharp instruments is essential (see Infobox 3) e.g. in post mortem examinations or the collection of human or animal brain/spinal cord
- remove protective clothing and wash hands before leaving the laboratory
- use closed systems such as sealed centrifuge buckets or where appropriate a Microbiological Safety Cabinet (MSC) to protect against splashing of material when mixing, centrifuging or homogenising samples
- use plastic single-use disposable items (containers, pipettes, inoculating loops and other such instruments); 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
- use recommended decontamination procedures – see Annex C

Cleaning and decontamination

3.14 As many of the standard methods of decontamination cannot ensure complete inactivation of TSE agents, the emphasis must be on the removal of the agent by thorough cleaning, followed by an appropriate autoclaving or liquid chemical treatment. Annex C gives detailed guidance on cleaning, decontamination and waste disposal.

Handling emergencies

3.15 There should be plans in place in the laboratory to deal with accidents involving TSE agents, for example dealing with spillages or first aid arrangements for inoculation injuries. Employees must report immediately to their employer, or any of their employer's other employees with specific responsibility for health and safety, any accident or incident that results in the release of a TSE agent. The training of employees working with TSEs should prepare them for this responsibility. The training should include highlighting the readily foreseeable incidents that could occur and the procedures for dealing with accidents, incidents and emergencies, and the name of the person or people to whom accidents should be reported.

3.16 Spillages should be handled according to the guidance in Annex C. Any inoculation injury or contamination of broken skin with TSE agents (or material that contains the agents) should be gently encouraged to bleed, washed (not scrubbed) with warm soapy water and covered with a waterproof dressing. Disinfectants should not be put onto cuts or broken skin, as this could impair the body's localised defence reaction to the injury.

3.17 An official local record should be kept of any incident or occurrence that involves exposure to TSE agents. Certain incidents will need to be reported to HSE under RIDDOR (see Part 2, paragraph 2.25).

Transport of specimens

3.18 All TSE-infected specimens of human and animal origin are classed as infectious substances for the purposes of transport. Guidance on the transport of this material is given in Annex D.

EXPERIMENTAL WORK WITH TSE AGENTS

3.19 As previously outlined, it may not be necessary to use all of the measures normally required at CL3 but any decision to dispense with certain CL3 containment measures should only be made on the basis of a local risk assessment (as described in paragraph 3.6 above). The assessment must be specific to the laboratory and the work that is being carried out.

3.20 Following a risk assessment, which may indicate that other risks require the use of full CL3 (for example, if other HG3 biological agents are likely to be present – see Table 3b), the main physical containment measures that might be dispensed with for experimental work are:

- The need for the laboratory to be sealable to permit fumigation, as the TSE agents are not affected by normal fumigants. Therefore, another means of decontamination for TSE agents, in particular in the event of a major spillage, will need to be addressed in a local code of practice/Standard Operating Procedure.

- It may not be necessary for the laboratory to be maintained at negative pressure. For example, if the work only involves the handling of small volumes of liquid, the work could be carried out within the confines of an appropriate microbiological safety cabinet – all such devices will have HEPA filtered exhausts. If a cabinet is used, consideration will need to be given to the routine disinfection of surfaces and also the action to be taken when the cabinet requires servicing. If, however the work involves activities that can spread contaminated material around and outside the laboratory, for example, block cutting, local exhaust ventilation may be required to control the spread of contaminated material. In addition, maintaining an inward airflow may further help to control the spread of contaminated material outside of the confines of the laboratory.

3.21 There may be certain experimental situations where the amount of TSE agents present is likely to be significantly higher than levels normally encountered in naturally occurring disease, or else the risk of exposure is increased because of certain activities, for example when material containing TSE agents is disrupted or concentrated by homogenisation or centrifugation. If this is the case, such situations should be carefully assessed and it may be necessary to work at full CL3.

DIAGNOSTIC LABORATORIES

3.22 A range of laboratory tests may be required for the clinical management of patients with known or suspected CJD. Similarly, veterinary diagnostic tests will be needed in herds where BSE may be known or suspected. Diagnostic-type tests may also be carried out on human or animal tissues for surveillance purposes (see Infobox 2).

3.23 Again, assessment may indicate that not all the containment measures normally required by CL3 are necessary. As before, the main containment measures that might not be required are the need for a sealable laboratory and the requirement for an inward airflow. The assessment must be specific to the laboratory that is undertaking the work, as sample processing procedures and equipment are likely to differ between laboratories.

3.24 Brain and spinal cord samples present the greatest risk of exposure to the TSE agent as compared to other diagnostic specimens and although certain containment measures may be dispensed with (as in paragraph 3.20), additional protective measures will need to be taken as follows:

- care should be taken to avoid accidental inoculation or injury, e.g. when preparing samples for microscopy or culture;
- disposable equipment should be used wherever practicable, e.g. cell counting chambers etc;
- any items contaminated by the specimens should be either destroyed by incineration, autoclaved or disinfected to the required standard (see Annex C for further details);
- any residual contamination of automated equipment should be minimised;
- any residual contamination of equipment should be dealt with before servicing;
- delicate equipment such as microscopes should be cleaned and maintained regularly to avoid accumulation of potentially contaminated debris.

3.25 It may be appropriate for the diagnostic analysis of all brain and neural tissue preparations from known, suspected and at risk patients or animals to be handled in a specialist neuropathology laboratory or centre.

Neuropathology

3.26 In addition to ensuring appropriate containment measures are taken for this type of work (as set out in paragraphs 3.20 and 3.24), it should be remembered that, although standard formalin is used for optimal fixation of whole brain for general histopathology purposes, formalin-fixed TSE tissue retain infectivity for long periods and should always be handled with the same precautions as fresh material. Similarly, tissue for electron microscopy fixed in glutaraldehyde retains its infectivity. Formalin-fixed TSE tissue can be decontaminated with formic acid treatment (Taylor DM, Brown JM, Fernie K and McConnell I, 1997) – see Annex C for details. (Formic acid treatment has not been shown to be effective for non-formalin-fixed material.) Once tissue blocks are fixed and formic acid-treated, sections can be cut on a standard microtome (preferably using a disposable knife) and processed as usual. Debris (wax shavings) from section cutting should be contained (see paragraph 3.20) and disposed of by incineration. The handling of archive material stored in fixative blocks or as mounted slides should also be subject to the same precautions as for fresh material.

Low risk specimens

3.27 This section of the guidance considers work with 'low' risk specimens (see Annex A.1 for infectivity of human tissues and Annex A.2 for animal tissues) such as CSF, blood, urine and faeces destined for routine clinical analysis. **This advice should not be interpreted as a means of carrying out any other work with TSE agents, or any other HG3 agents, under such conditions.** In addition to dispensing with measures outlined in paragraph 3.20 other CL3 requirements (above those needed at CL2) may be adapted to enable work on such specimens to take place in a CL2 laboratory. When preparing a risk assessment for work with low risk specimens the following points could be considered.

- The need to separate the work from other activities does not necessarily mean having a separate laboratory, although this would be the preferred solution. Work could be carried out at the beginning or end of a work period.

- If an observation window, or alternative to allow occupants to be seen is not available, then there will need to be some means of checking on staff, for example using CCTV or regular phone calls/agreed check-ins. Such measures will ensure that adequate supervision is in place when individuals are working alone.

- In terms of equipment used for the handling of infectious material, this should be disposable as far as possible or else cleaned thoroughly before being autoclaved.

- The transport of infectious material also needs to be considered. Ideally it should be stored within the room where it is to be handled. If this is not the case, it should be transported in robust, properly labelled, secured containers that should only be opened within the confines of a microbiological safety cabinet.

- Low risk specimens should be autoclaved prior to disposal by incineration; further guidance on decontamination and disposal of waste is given in Annex C.

- If a cabinet is used at CL2 to handle material, it should be remembered that although this means that the laboratory is under negative pressure to some extent, given that there is likely to be increased traffic in and out of such a laboratory, this negative pressure will not be constant and so the work should remain within the confines of a cabinet (see also guidance in 3.28 for work with low risk samples in autoanalysers).

Automated analysis of human clinical specimens

3.28 'Low' risk samples can be analysed in a fully enclosed automated system at CL2 providing any manual processing such as decanting is carried out within a microbiological safety cabinet. The low risk of infectivity together with the use of a fully enclosed system is considered sufficient to reduce any risk of exposure to the laboratory worker to a very low level. The assessment of these types of procedures should take into account whether:

- the system is fully enclosed and can contain spillage;
- waste can be disposed of without risk; and
- there are suitable maintenance and emergency procedures in place.

3.29 If the above cannot be ensured, then work should take place under the general conditions described in paragraph 3.27.

RESEARCH WORK WITH INFECTED ANIMALS

3.30 General guidance on laboratory work with infected animals is given in *Working safely with research animals: Management of infection risks.* In general, live animals infected with TSE agents do not pose a significant risk of exposure to TSE agents. However, the nature of experimental work with such animals means that there will be procedures/tasks that increase the risk of exposure. Work with specified risk material (SRM) or TSE agents in live animals may require a license (The TSE (England) Regulations 2002).

3.31 There are certain minimum containment requirements for work with animals experimentally infected with TSE agents, as shown in Table 3a. Small animal work

includes work with, for example poultry, rodents, rabbits, mink, cats and dogs. Large animal work includes work with, for example, domestic farm animals such as sheep and cattle.

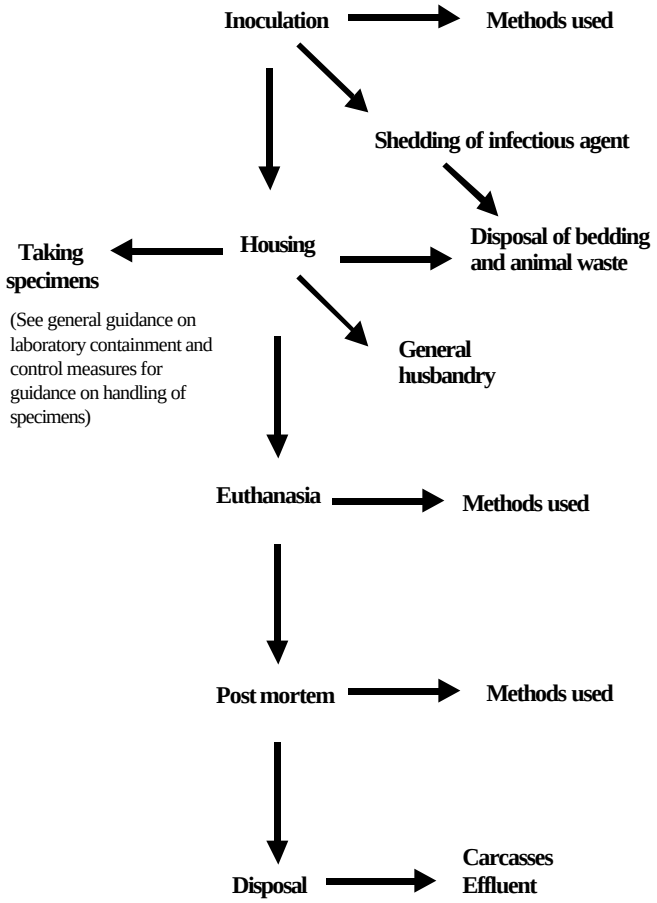
3.32 Generally, the rationale for work with small animals requiring more stringent containment measures than large animals is because of the increased likelihood of biting and scratching when working with such animals. But, as with experimental laboratory work with TSE agents, a local assessment of work at Animal Containment Level 3 may indicate that not all the measures normally required are necessary to control exposure i.e. the room need not be sealable to permit fumigation. The risk of exposure when working with live large animals such as sheep and cattle is considered remote and Animal Containment Level 1 is appropriate. Where experimental sheep, goats and cattle are pregnant, guidance in paragraph 3.44 should be taken into account in planning for parturition or caesarean section.

3.33 Having identified the appropriate containment level for the work, the local risk assessment of the work must identify all potential exposure points to determine whether other additional precautions are required to control exposure, in particular for work with large animals. Additional precautions may also be required, for example, when concentrations of infectivity above those found naturally might be expected.

3.34 Potential points of exposure are illustrated in Figure 3.1, with further guidance given in paragraphs 3.36 to 3.47.

3.35 Having completed the risk assessment, local rules/standard operating procedures should then be prepared detailing safe working practices.

Figure 3.1: points to consider in assessment



Restraint

3.36 For procedures such as inoculation of infectious material and taking of blood, the need for sedation of the experimental animal should be considered to protect staff from injury. If the animal is not to be sedated, the animal should be appropriately restrained and procedures should not be carried out by lone workers. Adult cattle infected with TSE agents can be especially unpredictable and work should only be carried out by experienced staff.

Inoculation

3.37 The route of inoculation of infectious material should be assessed to determine whether this would allow leakage of this material post-inoculation and if this could contaminate bedding etc.

3.38 When infecting by injection, leakage from the injection site should be controlled and any leakage should be soaked up with absorbent material that should be treated as clinical waste. Sealants could also be applied to the wounds to control contamination of bedding etc.

3.39 Consideration should be given to whether inoculum remains exposed for any period of time, as may be the case when using feed as the source of infection.

3.40 As there is potential for excretion of infectious material post inoculation especially when infection is via the oral route (albeit for a limited period of time) (Dickinson AG and Taylor DM, 1978) then faecal waste and material contaminated by waste, e.g. bedding, should be collected and disposed of by incineration for at least 4 weeks post-inoculation.

Husbandry

3.41 Certain tasks with large animals such as foot trimming, ear tagging, and shearing of sheep may create a risk of exposure to blood and other body fluids. Given the potential for transmission of infection via blood (Hunter N *et al*, 2002), appropriate precautions should be taken to avoid exposure to blood and accidental puncture wounds. For example, wearing of appropriate personal protective equipment such as gloves which should be cut resistant (NB: cut resistant gloves do not offer protection from penetrating injuries – see Infobox 3), immediate disposal of needles when administering veterinary treatment and face protection if there is a possibility of exposure to blood under pressure coming into contact with mucous membranes such as the eyes.

3.42 The housing of small animals will need to balance the need for positive pressure, for example to maintain a germ-free environment or else protect immunosuppressed animals, against the need for inward flow of air at CL3. In such cases the use of simple engineering controls (e.g. flexible barriers) or respiratory protective equipment (RPE) may be necessary and should be addressed in the local risk assessment.

Infobox 3: Protective gloves

Gloves or other hand protection should be capable of giving protection from hazards, be comfortable and fit the wearer. The choice should be made on the basis of suitability for protection, compatibility with the work and the requirements of the user. The ability of the gloves to resist abrasion and other industrial wear and tear should be considered and the manufacturer's instructions and markings for appropriate use and level of protection should be followed. When selecting gloves for chemical protection, reference should be made to chemical permeation and resistance data provided by manufacturers.

Gloves made from chain-mail or leather and metal or plastic arm guards offer some protection against stabs and are used in those aspects of work where a knife is moved towards the user's hand and forearm. Gloves knitted from special man-made fibres such as Kevlar will provide protection against cuts and gloves manufactured from, e.g. Kevlar needlefelt, give good puncture resistance.

See also BS EN 374:1994 (Parts 1-3) *Protective gloves against chemicals and micro-organisms,* BS EN 388:1994 *Protective gloves against mechanical risks* and BS EN 1082-1:1997 *Protective clothing. Gloves and arm guards protecting against cuts and stabs by hand knives. Chain mail gloves and arm guards* for further information.

Collection of specimens

3.43 The type of sample required will affect the control measures required. Taking of blood specimens should be carried out so as to avoid exposure to blood and accidental puncture wounds, e.g. wearing of appropriate personal protective equipment and immediate disposal of needles (needles should not be resheathed). Face protection may be necessary if there is a possibility of exposure to blood under pressure coming into contact with mucous membranes such as the eyes and the mouth.

Parturition

3.44 As there is the possibility of maternal transmission in sheep and a risk in cattle that cannot be discounted (Race, Jenny & Sutton, 1998; Onodera, Ikeda, Muramatsu & Shinagua, 1993; Pattison, Hoare, Jebbet & Watson, 1972) infected animals should give birth in a separate area and all non-viable products of parturition, e.g. placentae and any contaminated bedding etc disposed of via incineration. The area should be cleaned and disinfected after use with sodium hypochlorite (20,000 ppm available chlorine) for 1 hour. Staff attending large animals should wear appropriate protective clothing, i.e. parturition gown, gloves, face shield/mask. Where experimental animals are intended to be exposed to potential contaminating material at or around the time of birth, the above guidelines can be modified provided that a risk assessment is performed and appropriate measures are taken to control exposure.

Disposal of waste

3.45 Carcasses and other associated material, e.g. tissue samples, from all animals experimentally infected with a TSE agent should be disposed of by incineration. Bedding and faecal waste (following any initial shedding phase) can be disposed of in the normal way *(*e.g. by landfill burial, spreading on land or discharge to the sewer system) subject to the requirements of DEFRA, the Environment Agency [EA] and the Local Authority. (For further information see the duty of care under section 34 of the Environmental Protection Act 1990 on passing clinical waste to a registered carrier for disposal – note, the EA are still consulting on technical guidance to support this legislation.)

Post mortem examination

3.46 Before post mortem examinations are performed on animals naturally or experimentally infected with a TSE agent, an assessment should be made of the necessity for the procedure.

3.47 The control hierarchy set out in COSHH (see COSHH ACoP and Guidance) requires that exposure be prevented in the first instance. The following points should be addressed when drawing up local codes of practice.

a) The Containment Level of the post mortem area must be 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.

b) 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); only essential persons should be present in the post mortem room when carrying out procedures with infected animals.

c) At least 2 persons should be present; in addition a circulator should attend (remaining uncontaminated) acting as an observer and co-ordinator, for example taking care of record-keeping, and handing over sterile/clean instruments etc.

d) Consideration should be given to the subsequent disinfection of working surfaces, for example, work with small animals may be conducted in a stainless steel or plastic tray (enamel trays are not recommended) which should be washed clean before being autoclaved[1] or disinfected with hypochlorite (20,000 ppm available chlorine) for 1 hour. Disposable coverings should protect other working surfaces.

e) For large animal post mortems, consideration should be given to the means by which blood, body fluids and tissues that may be discarded during the post mortem examination will be collected and disposed of safely.

f) Single-use disposable items should be used wherever practicable (alternatively a set(s) of dedicated instruments may be used) and appropriate protective clothing, including gloves, gowns, footwear, masks and visors or safety spectacles, should be worn. For large animal post mortems, heavy duty or waterproof clothing should be used. All items of reusable clothing should be rinsed clean in the post mortem suite before being autoclaved[1]. For items that would not withstand repeated autoclaving such as rubberised boots, these should be washed clean then disinfected using hypochlorite (20,000 ppm available chlorine). All disposable clothing should be autoclaved before being disposed of by incineration.

g) Carcases should be double bagged and placed in sealable bins prior to disposal by incineration. Small animal carcasses should be autoclaved prior to incineration.

([1] although autoclaving will not completely remove the TSE agent it will reduce the level of infectivity and also eliminate any other infectious agents that may be present on contaminated surfaces or clothing.)

Use of specified risk material (SRM) in research

3.48 Those carrying out non-TSE research work should be aware certain animal tissues are designated SRM and subject to The TSE (England) Regulations 2002. If this is the case the material (e.g. bovine eyes from UK cattle over 6 months old) should not be

sourced from cattle slaughtered under the purchase scheme introduced under EC Regulation 716/96 or at the request of the Secretary of State to prevent BSE, to reduce the risk of exposure to TSE agents. If SRM is used for non-TSE research purposes it should not be allowed to come into contact with other non-SRM; particularly it must be kept in premises free from food, feedingstuffs, cosmetics, pharmaceuticals, medical products, their starting materials or intermediate products. A licence may be required from the Secretary of State to conduct research with SRM. COSHH requires a minimum of CL2 in laboratories that do not intentionally work with biological agents but handle materials in respect of which there exist uncertainties about the presence of Hazard Group 2, 3 or 4 biological agents. Even if there is a negligible risk from BSE in such material, it may contain other zoonotic agents, hence CL2 would be appropriate.

References for Part 3:

Legislation:

The Control of Substances Hazardous to Health Regulations 2002. SI 2002/2677. The Stationary Office. ISBN 0 11 042919 2.

The Reporting of Incidents, Diseases and Dangerous Occurrences Regulations 1995. SI 1995/3163. The Stationary Office. ISBN 01 1053 7523.

The TSE (England) Regulations 2002. SI 2002/843. The Stationery Office. ISBN 0 11 039914 5.

The Environmental Protection Act 1990. c. 43. The Stationery Office. ISBN 0 1054 4390 5

Commission Regulation No.716/96 of 19 April 1996 adopting exceptional support measures for the beef market in the United Kingdom.

Guidance:

Advisory Committee on Genetic Modification's Compendium of Guidance. Available at www.hse.gov.uk/hthdir/noframes/acgmcomp/acgmcomp.htm & HSE Books 2000 ISBN 0 7176 1763 7

HSC's Approved List of Biological Agents, also known as *Second supplement to "Categorisation of biological agents according to hazard and categories of containment"* (MISC 208) Available at www.hse.gov.uk/hthdir/noframes/agent1.pdf & HSE Book 2000. ISBN 0717620344

Control of Substances Hazardous to Health (Fourth edition). The Control of Substances Hazardous to Health Regulations 2002. Approved Code of Practice and Guidance (L5) HSE Books 2002. ISBN 0 7176 2534 6 (A priced publication)

Management, design and operation of microbiological containment laboratories. HSE Books 2001. ISBN 0 7176 2034 4. (A priced publication)

Working safely with research animals: Management of infection risks.

HSE Books 1997. ISBN 0 7176 1377 1 (A priced publication)

BS EN 374:1994 Protective gloves against chemicals and micro-organisms.

BS EN 388:1994 Protective gloves against mechanical risks.

BS EN 1082-1:1997 Protective clothing. Gloves and arm guards protecting cuts and stabs by hand knives. Chain mail gloves and arm guards.

Information on Environmental Protection Act 1990 available at www.environment-agency.gov.uk/subjects/waste

Articles:

Matthews, D (2003) Pers. comm. Data on incidences of BSE in cattle in 2001 and 2002 (e-mail).

Taylor DM, Brown JM, Fernie K and McConnell I (1997) The effect of formic acid on BSE and scrapie infectivity in fixed and unfixed brain tissue. Veterinary Microbiology, Vol 58, 167-174.

Dickinson AG and Taylor DM (1978) Resistance of scrapie agent to decontamination. New England Journal of Medicine, Vol 299, 1413-1414.

Hunter N, Foster J, Chong A, McCutcheon S, Parnham D, Eaton S, MacKenzie C, and Houston F. (2002) Transmission of prion diseases by blood transfusion. Journal of General Virology, Vol 83 (11), 2897-2905

Race R, Jenny A and Sutton D (1998) Scrapie infectivity and Proteinase K-resistant prion protein in sheep placenta, brain, spleen and lymph node: implications for transmission and antemortem diagnosis. Journal of Infectious Diseases, Vol 178, 949-953.

Onodera T, Ikeda T, Muramatsu Y and Shinagua M (1993) Isolation of scrapie agent from the placenta of sheep with natural scrapie in Japan. Microbiological Immunology, Vol 37(4), 311-316.

Pattison IH, Hoare MN, Jebbet JN and Watson WA (1972) Spread of scrapie to sheep and goats by oral dosing with foetal membranes from scrapie-infected sheep. Veterinary Record, Vol 90, 465.

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PART 4

INFECTION PREVENTION AND CONTROL OF CJD and VARIANT CJD IN HEALTHCARE AND COMMUNITY SETTINGS

Summary of advice

Part 4 provides advice on safe working practices with the aim of preventing the transmission of CJD and other human prion diseases in hospital and community healthcare settings

Note: Variably Protease-Sensitive Prionopathy (VPSPr)

i) VPSPr is a recently described human prion disease, which appears to be a rare sporadic disorder affecting patients in an age range similar to those affected by sporadic CJD.

ii) VPSPr is transmissible experimentally to transgenic mice expressing varying levels of the human prion protein, but the results suggest that the potential for human to human transmission may be limited[1,2]. The transmission characteristics of VPSPr are different from those of sporadic CJD and variant CJD in the transgenic mice studied.

iii) There is very little data on the detection of abnormal prion protein outside the CNS in VPSPr, so as for other prion diseases where these data are lacking (e.g. many genetic forms of prion disease) it seems reasonable to assume a similar tissue distribution to sporadic CJD, since there is no evidence to indicate that VPSPr is a BSE-related disorder.

iv) Further advice on VPSPr can be obtained from NCJDRSU (Professor James Ironside or Dr Anna Molesworth).

[1] Diack *et al.* 2014.Variably Protease-Sensititve Prionopathy, a Unique Prion Variant with Inefficient Transmission Properties. *Emerging Infectious Diseases* 12, 1969-79.

[2] Notari *et al.* 2014. Transmission Characteristics of Variably Protease-Sensitive Prionopathy. *Emerging Infectious Disesases* 12, 2006-14.

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Previous revision date: January 2014
Changes new to this edition:

Date	Change	Notes
February 2015	Change of terminology from 'CJD or vCJD' to 'CJD', for simplicity.	Changed throughout the document as appropriate.
February 2015	Note on VPSPr updated	This change affects the information box on the first page.
February 2015	Description of the use of the term CJD updated	This change affects paragraph 4.2.
February 2015	Addition of information on where advice can be sought.	Paragraph 4.4 has been added.
February 2015	Clarification that the Health and Social Care Act 2008 covers England only.	This change affects paragraph 4.7.
February 2015	Reference to the CJD Incidents Panel removed, as this Panel no longer exists.	This change affects paragraph 4.18.
February 2015	Reference to Department of Health's 'Transmissible spongiform encephalopathy: Safe working and the prevention of infection' removed, as this document is no longer available.	This change affects paragraph 4.36
February 2015	Additional guidance for single-use instruments.	This change affects the first bullet point in paragraph 4.47.
February 2015	Addition of a section about problems with surgical instruments.	Paragraph 4.56 has been added.

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CONTENTS

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Introduction

4.1 This guidance provides advice on safe working practices with the aim of preventing the transmission of CJD and variant CJD (vCJD) in hospital and community healthcare settings.

4.2 The use of the term "CJD" in this guidance encompasses sporadic CJD, sporadic fatal insomnia, variable protease-sensitive prionopathy (VPSPr), vCJD, iatrogenic CJD, genetic CJD, Fatal Familial Insomnia (FFI) and Gerstmann-Straussler-Scheinker Disease (GSS), in order to assist readability.

4.3 In this guidance document, the term 'patients with, or "at increased risk" of, CJD' is used as a proxy for all patient groups in Table 4a. Where this term is used, the guidance is applicable to all patient groups in this Table.

4.4 Advice is available from the Public Health England CJD Section, who can be contacted on 020 8327 6090.

Other relevant guidance

Caring for patients with, or "at increased risk" of, CJD

4.5 "Creutzfeldt-Jakob Disease: Guidance for Healthcare Workers" advice on the care of patients with CJD is available at http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4082370.pdf. This document refers to a "key worker" who will be constantly involved in the co-ordination of care of a patient with a clinical diagnosis of CJD, in either a hospital or community setting. This is a named professional with a good knowledge of local health and social services, who should be identified as soon as possible after a diagnosis of CJD seems likely. The "key worker" will provide continuing support and be the primary source of advice and information, to both the patient and their family, and act as a patient advocate for necessary resources. Practical advice on developing patient care packages can be obtained from the National Care Team (http://www.cjd.ed.ac.uk/care.html) at the National

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CJD Research and Surveillance Unit, Western General Hospital, Crewe Road, Edinburgh, telephone number 01313 537 1980.

4.6 Guidance from the vCJD Clinical Governance Advisory Group, available here, recommends that GPs should remain the patient's clinical guardian and anchor, supported by consultant neurologists and the specialist national centres – the National CJD Research and Surveillance Unit and the National Prion Clinic.

Management arrangements for infection prevention and control

4.7 Under the Health and Social Care Act 2008, NHS bodies in England have to register with the Care Quality Commission (CQC), and as a requirement of registration they must protect patients, workers and others who may be at risk of acquiring a healthcare-associated infection (including CJD).

4.8 The 2008 Act enables the Secretary of State for Health to issue a Code of Practice relating to healthcare-associated infections and the CQC to assess compliance with registration requirements on cleanliness and infection prevention and control by reference to this Code. A revised 'Code of Practice on the prevention and control of infections and related guidance' was published in January 2011: https://www.gov.uk/government/publications/the-health-and-social-care-act-2008-code-of-practice-on-the-prevention-and-control-of-infections-and-related-guidance

4.9 The Code of Practice applies to registered providers of all healthcare and adult social care in England. This includes NHS bodies, independent providers, primary dental care providers, independent sector ambulance providers and primary medical care providers

4.10 The Code of Practice supersedes 'Standards for Better Health' and Controls Assurance standards.

4.11 The Code of Practice does not replace the requirement to comply with any other legislation that applies to health and social care services; for example, the Health

and Safety at Work *etc*. Act 1974, and the Control of Substances Hazardous to Health Regulations 2002.

Tissue infectivity

4.12 Annexes A1 and A2 provide a summary of the distribution of abnormal prion protein in human tissues, a classification of infectivity in human tissues and body fluids in CJD, based (where available) on data from experimental studies, and a summary of information from other studies of natural transmissible spongiform encephalopathy (TSE) diseases in humans and animals.

Iatrogenic transmission

4.13 There is no evidence to suggest that CJD is spread from person to person by close contact, though it is known that transmission of CJD can occur in specific situations associated with medical interventions – iatrogenic infections. Due to the possibility of iatrogenic transmission of CJD, precautions need to be taken for certain procedures in healthcare, to prevent transmission.

CJD (except vCJD)

4.14 Worldwide, cases of iatrogenic CJD have been associated with the administration of hormones prepared from human pituitary glands and *dura mater* preparations, and one case has been reported associated with a corneal graft (it is possible that the corneal tissue was contaminated by posterior segment tissue during processing). Iatrogenic transmission has also been identified following neurosurgical procedures with inadequately decontaminated instruments or EEG needles.

vCJD

4.15 There have been no known transmissions of vCJD via surgery or use of tissues or organs. Since 2003, four cases (three clinical and one asymptomatic) of presumed person-to-person transmission of vCJD infection via blood transfusion of non-leucodepleted red blood cells have been reported in the UK. In addition, in 2009, a case of probable asymptomatic vCJD infection via plasma products was reported in a haemophiliac.

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4.16 Since 1997, when the theoretical risk of vCJD transmission through blood was first considered, the UK blood services have taken a number of precautionary measures to protect the blood supply and associated plasma products. These precautionary measures to reduce the risk include:

- Blood components, plasma products or tissues obtained from any individual who later develops vCJD are withdrawn/recalled to prevent their use;
- Plasma for the manufacture of plasma products, such as clotting factors, has been obtained from non-UK sources since 1998;
- Synthetic (recombinant) clotting factor for treatment of haemophilia has been provided to those aged under 16 since 1998, and for all patients in whom it is suitable since 2005;
- Since 1999 white blood cells (which may carry a significant risk of transmitting vCJD) have been reduced in all blood used for transfusion, a process known as leucodepletion;
- Since 2002, fresh frozen plasma for treating babies and young children born on or after 1 January 1996 has been obtained from the USA. In 2005 its use was extended to all children up to the age of 16;
- Since 2004, individuals who have received a transfusion of blood components since January 1980, or are unsure if they have had a blood transfusion, are excluded from donating blood or platelets;
- Since 2009, cryoprecipitate, a special cold-treated plasma preparation, has been imported from the USA for children up to the age of 16.

Patient categorisation

4.17 When considering measures to prevent transmission to patients or staff in the healthcare setting, it is useful to make a distinction between:

- symptomatic patients, *i.e.* those who fulfil the diagnostic criteria for definite, probable or possible CJD (see Annex B for full diagnostic criteria), and;
- patients “at increased risk” *i.e.* those with no clinical symptoms, but who are “at increased risk” of developing CJD, because of their family or medical history. For this group of patients, the infection prevention and control advice differs in some circumstances for:

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- Patients at increased risk of genetic CJD
- Patients at increased risk because they have received blood from an individual who later developed variant CJD
- Other patients at increased risk of iatrogenic CJD

Table 4a details the classification of the risk status of symptomatic patients and patients “at increased risk”.

Patients “at increased risk” of CJD

4.18 A number of patients have been identified as “at increased risk” due to a medical or family history which places them “at increased risk” of developing CJD. These patient groups are outlined in Table 4a.

4.19 In most routine clinical contact, no additional precautions are needed for the care of patients in the “at increased risk” patient groups. However, when certain invasive interventions are performed, there is the potential for exposure to the agents of TSEs. In these situations it is essential that control measures are in place to prevent iatrogenic CJD transmission.

4.20 All people who are “at increased risk” of CJD are asked to help prevent any further possible transmission to other patients by following this advice:

- Don’t donate blood. No-one who is “at increased risk” of CJD, or who has received blood donated in the United Kingdom since 1980, should donate blood;
- Don’t donate organs or tissues, including bone marrow, sperm, eggs or breast milk;
- If you are going to have any medical, dental or surgical procedures, tell whoever is treating you beforehand so they can make special arrangements for the instruments used to treat you if you need certain types of surgery or investigation;
- You are advised to tell your family about your increased risk. Your family can tell the people who are treating you about your increased risk of CJD if you need medical or surgical procedures in the future and you are unable to tell them yourself.

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Table 4a: Categorisation of patients by risk

	Patient groups
Symptomatic patients	• Patients who fulfill the diagnostic criteria for definite, probable or possible CJD (see Annex B for diagnostic criteria) • Patients with neurological disease of unknown aetiology, who do not fit the criteria for possible CJD, but where the diagnosis of CJD is being actively considered
Patients "at increased risk" from genetic forms of CJD	• Individuals who have been shown by specific genetic testing to be at significant risk of developing CJD. • Individuals who have a blood relative known to have a genetic mutation indicative of genetic CJD; • Individuals who have or have had two or more blood relatives affected by CJD or other prion disease
Patients identified as "at increased risk" of vCJD through receipt of blood from a donor who later developed vCJD	• Individuals who have received labile blood components (whole blood, red cells, white cells or platelets) from a donor who later went on to develop vCJD.
Patients identified as "at increased risk" of CJD through iatrogenic exposures	• Recipients of hormone derived from human pituitary glands, *e.g*. growth hormone, gonadotrophin, are "at increased risk" of transmission of sporadic CJD. In the UK the use of human-derived gonadotrophin was discontinued in 1973, and use of cadaver-derived human growth hormone was banned in 1985. However, use of human-derived products may have continued in other countries after these dates. • Individuals who underwent intradural brain or intradural spinal surgery before August 1992 who received (or might have received) a graft of human-derived dura mater are "at increased risk" of transmission of sporadic CJD (unless evidence can be provided that human-derived dura mater was not used). • Individuals who have had surgery using instruments that had been used on someone who went on to develop CJD, or was "at increased risk" of CJD; *Continued overleaf*

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	• Individuals who have received an organ or tissue from a donor infected with CJD or "at increased risk" of CJD; • Individuals who have been identified as having received blood or blood components from 300 or more donors since January 1990; • Individuals who have given blood to someone who went on to develop vCJD; • Individuals who have received blood from someone who has also given blood to a patient who went on to develop vCJD; • Individuals who have been treated with certain implicated UK sourced plasma products between 1990 and 2001

4.21 GPs are asked to record their patient's CJD risk status in their primary care records. The GP should also include this information in any referral letter should the patient require surgical, medical or dental procedures.

4.22 Recipients of ocular transplants, including corneal transplants, are not considered to be "at increased risk" of CJD.

Hospital care of CJD patients

4.23 There is no evidence that normal social or routine clinical contact with a CJD patient presents a risk to healthcare workers, relatives or others. Isolation of patients with CJD is not necessary, and they can be nursed in an open ward using standard infection prevention and control precautions in line with those used for all other patients.

Sample-taking and other invasive medical procedures

4.24 When taking samples or performing other invasive procedures, the possible infectivity of the tissue(s) involved must be considered, and if necessary suitable precautions taken. Information on tissue infectivities for CJD is included in Annex A1 of this guidance. **It is important to ensure that only trained staff, who are aware of the hazards, carry out invasive procedures that may lead to contact with medium or high risk tissue.**

4.25 Body secretions, body fluids (including saliva, blood, cerebrospinal fluid [CSF] and excreta) are all low risk for CJD. It is therefore likely that the majority of

samples taken or procedures performed will be low risk. Contact with small volumes of blood (including inoculation injury) is considered low risk, though it is known that transfusion of large volumes of blood and blood components may lead to vCJD transmission.

4.26 Blood and body fluid samples from patients with, or "at increased risk" of, CJD should be treated as potentially infectious for blood-borne viruses and handled with standard infection prevention and control precautions as for any other patient, *i.e.*;

- use of disposable gloves and eye protection where splashing may occur;
- avoidance of sharps injuries and other forms of parenteral exposure;
- safe disposal of sharps and contaminated waste in line with locally approved arrangements; and
- single-use disposable equipment should be used wherever practicable.

4.27 When taking biopsy specimens of medium or high risk tissue, for example tonsil biopsy in a patient with suspected vCJD, or intestinal biopsy in a patient "at increased risk" of vCJD, every effort should be taken to minimise the risk of infecting the operator or contaminating the environment.

4.28 In the event of needing to consider a brain biopsy, advice from the Department of Health, endorsed by the Chief Medical Officer, is available in Annex I.

4.29 Samples from patients with, or "at increased risk" of, CJD should be marked with a 'Biohazard' label, and it is advisable to inform the laboratory in advance that a sample is being sent.

Spillages

4.30 When a spillage of <u>any</u> fluid (including blood and CSF) from a patient with, or "at increased risk" of, CJD occurs in a healthcare setting, the main defence is efficient removal of the contaminating material and thorough cleaning of the surface.

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4.31 Standard infection prevention and control precautions should be followed for any spillages, which should be cleared up as quickly as possible, keeping contamination to a minimum. Disposable gloves and an apron should be worn when removing such spillages.

4.32 For spillages of large volumes of liquid, absorbent material should be used to absorb the spillage, for which a number of proprietary absorbent granules are available.

4.33 Standard disinfection for spillages (eg. 10,000ppm chlorine-releasing agent) should be used to decontaminate the surface after the spillage has been removed. A full risk assessment may be required. It should be noted that none of the methods currently suggested by WHO for prion inactivation are likely to be fully effective.

4.34 Any waste (including cleaning tools such as mop heads, and PPE worn) should be disposed of as clinical waste (see below and Table 4b).

Clinical waste

4.35 General guidance on the safe management of clinical waste is given in the Department of Health's guidance document 'Health Technical Memorandum 07-01: Safe Management of Healthcare Waste', available at: https://www.gov.uk/government/publications/guidance-on-the-safe-management-of-healthcare-waste.

4.36 According to this guidance, "Waste known or suspected to be contaminated with transmissible spongiform encephalopathy (TSE) agents, including CJD, must be disposed of by high temperature incineration in suitable authorised facilities."

4.37 The ACDP TSE Sub Group have considered the disposal of clinical waste, and have agreed that tissue and contaminated materials such as dressings and sharps, from patients with, or "at increased risk" of, CJD, should be disposed of as in Table 4b.

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Table 4b: Disposal of clinical waste from patients with, or "at increased risk" of, CJD

Diagnosis	High or medium risk tissue*	Low risk tissue and body fluids**
Definite	Incinerate	Normal clinical waste disposal
Probable	Incinerate	Normal clinical waste disposal
"At increased risk"	Incinerate	Normal clinical waste disposal

** See Annex A1*

*** Tissues and materials deemed to be low risk include body fluids such as urine, saliva, sputum, blood, and faeces. Blood from vCJD patients is considered to be low risk except when transfused in large volumes.*

Childbirth

4.38 In the event that a patient with, or "at increased risk" of, CJD becomes pregnant, it is important to ensure that patient confidentiality is properly maintained, and that any action taken to protect public health does not prejudice individual patient care.

4.39 Childbirth should be managed using standard infection prevention and control procedures. The placenta and other associated material and fluids are designated as low risk tissues, and should be disposed of as clinical waste, unless they are needed for investigation, in which case the precautions outlined in paragraphs 4.24-4.29 above should be followed. Instruments should be handled following the advice in paragraphs 4.46-4.56 below.

Bed linen

4.40 Used or fouled bed linen (contaminated with body fluids or excreta), should be washed and dried in accordance with current standard practice. No further handling or processing is necessary.

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Occupational exposure

4.41 Although cases of CJD have been reported in healthcare workers, there have been no confirmed cases linked to occupational exposure. However, it is prudent to take a precautionary approach.

4.42 The highest potential risk in the context of occupational exposure is from exposure to high infectivity tissues through direct inoculation, for example as a result of sharps injuries, puncture wounds or contamination of broken skin, and exposure of the mucous membranes.

4.43 Healthcare personnel who work with patients with definite, probable or possible CJD, or with potentially infected tissues, should be appropriately informed about the nature of the risk and relevant safety procedures.

4.44 Compliance with standard infection prevention and control precautions, in line with those set out in "Guidance for Clinical Health Care Workers: Protection Against Infection with Blood-borne Viruses" recommended by the Expert Advisory Group on AIDS and the Advisory Group on Hepatitis will help to minimise risks from occupational exposure.

4.45 For any accident involving sharps or contamination of abrasions with blood or body fluids, wounds 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. Splashes into the eyes or mouth should be dealt with by thorough irrigation. The accident should be reported as defined in local practice, and an accident or incident form completed.

Surgical procedures and instrument management

4.46 For all patients with, or "at increased risk" of, CJD, the following precautions should be taken for surgical procedures:

- Wherever appropriate and possible, the intervention should be performed in an operating theatre;

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- Where possible, procedures should be performed at the end of the list, to allow normal cleaning of theatre surfaces before the next session;
- Only the minimum number of healthcare personnel required should be involved;
- Protective clothing should be worn, *i.e.* liquid repellent operating gown, over a plastic apron, gloves, mask and goggles, or full-face visor;
    - for symptomatic patients, this protective clothing should be single-use and disposed of in line with local policies;
    - for patients "at increased risk" of CJD, this protective clothing need not be single-use and may be reprocessed;
- Single-use disposable surgical instruments and equipment should be used where possible, and subsequently destroyed by incineration or sent to the instrument store;
- Effective tracking of reusable instruments should be in place, so that instruments can be related to use on a particular patient.

Single-use instruments

4.47 Single-use instruments are utilised variably across surgical specialities and NHS Trusts. The following should be taken into account when using single-use instruments:

- The quality and performance of single-use instruments should be equivalent to those of reusable instruments with appropriate procurement, quality control and audit mechanisms in place. This should include assessment of residual post-production organic contamination;
- Procurement should be quality-based not cost-based, with the minimum safe functional requirements of each instrument purchased being understood by the purchaser;
- For reusable instruments there is an internal quality control, with instruments noted as faulty being either repaired or returned to the system manufacturer. A similar process needs to be put in place for any single-use instrument that is purchased;

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- A CE mark is not necessarily a mark of quality of instruments, and quality-control of sub-contractors is often difficult when the number of instruments increases.

Handling of instruments that are not designated as single-use

4.48 Where single-use instruments are not available, the handling of reusable instruments depends on:

- how likely the patient is to be carrying the infectious agent (the patient's risk status);
- whether the patient has, or is "at increased risk" of, CJD; and
- how likely it is that infection could be transmitted by the procedure being carried out *i.e.* whether there is contact with tissues of high or medium infectivity.

4.49 Tables 4c and 4d separately set out the actions to be taken for instruments used on patients with or "at increased risk" of CJD. The differences in instrument management are due to differences in tissue infectivities between CJD and vCJD. These actions are also summarised in the algorithm at the end of this document.

Quarantining instruments

4.50 Annex E provides guidance on the procedures that should be followed when quarantining surgical instruments is considered.

Decontamination of instruments

4.51 **Effective decontamination is key to reducing the risk of transmission of CJD through surgery.** Annex C contains advice on the general principles of decontamination for TSE agents, and Table C3 contains a list of selected guidelines and standards related to decontamination.

4.52 It is important that the efficacy, safety, and compatibility with other decontamination processes of products and technologies claiming to remove or inactivate prion protein from contaminated medical devices in laboratory and

clinical practice, is established. Until this occurs, clinicians and laboratory managers should ensure that current guidelines are followed.

Table 4c: Handling of instruments – patients with, or "at increased risk" of, CJD (other than vCJD)

Tissue Infectivity	Status of patient		
	Definite or probable	**Possible**	**At increased risk**
High* Brain Spinal cord Cranial nerves, specifically the entire optic nerve and the intracranial components of the other cranial nerves Cranial ganglia Posterior eye, specifically the posterior hyaloid face, retina, retinal pigment epithelium, choroid, subretinal fluid and optic nerve Pituitary gland	single-use or Destroy or Quarantine for re-use exclusively on the same patient	single-use or Quarantine for re-use exclusively on the same patient pending diagnosis	Single-use or Destroy or Quarantine for re-use exclusively on the same patient
Medium Spinal ganglia Olfactory epithelium	Single-use or Destroy or Quarantine for re-use exclusively on the same patient	Single-use or Quarantine for re-use exclusively on the same patient pending diagnosis	Single-use or Destroy or Quarantine for re-use exclusively on the same patient
Low	No special precautions	No special precautions	No special precautions

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Table 4d: Handling of instruments – patients with, or "at increased risk" of vCJD

Tissue Infectivity	Status of patient		
	Definite or probable	**Possible**	**At increased risk**
High* Brain Spinal cord Cranial nerves, specifically the entire optic nerve and the intracranial components of the other cranial nerves Cranial ganglia Posterior eye, specifically the posterior hyaloid face, retina, retinal pigment epithelium, choroid, subretinal fluid and optic nerve Pituitary gland	Single-use or Destroy or Quarantine for re-use exclusively on the same patient	Single-use or Quarantine for re-use exclusively on the same patient pending diagnosis	Single-use or Destroy or Quarantine for re-use exclusively on the same patient
Medium Spinal ganglia Olfactory epithelium Tonsil Appendix Spleen Thymus Adrenal gland Lymph nodes and gut-associated lymphoid tissues	Single-use or Destroy or Quarantine for re-use exclusively on the same patient	Single-use or Quarantine for re-use exclusively on the same patient pending diagnosis	Single-use or Destroy or Quarantine for re-use exclusively on the same patient
Low	No special precautions	No special precautions	No special precautions

*Although dura mater is designated low infectivity tissue, procedures conducted on intradural tissues (*i.e.* brain, spinal cord and intracranial sections of cranial nerves) or procedures in which human dura mater has been implanted in a patient prior to 1992, are high risk and instruments should be handled as such.

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Incineration of instruments

4.53 The instruments should already be in a combustible sealed container. This should then be disposed of via the clinical waste stream, ensuring that this results in incineration.

Complex instruments

4.54 Some expensive items of equipment, such as drills and operating microscopes, may be prevented from being contaminated by using shields, guards or coverings, so that the entire item does not need to be destroyed. In this case, the drill bit, other parts in contact with high or medium risk tissues, and the protective coverings, 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.

Use of laser for tonsillectomy – smoke plumes

4.55 Some ENT surgeons may use laser techniques as an alternative to 'conventional' surgery for tonsillectomy. There is no evidence of the transmission of TSEs by the respiratory route. Any risk to surgeons from smoke plumes is thought to be very low, but there are no data on vCJD. General guidance on the safe use of lasers is available from Medicines and Healthcare products Regulatory Agency (MHRA) - Device Bulletin 2008(03) 'Guidance on the safe use of lasers, intense light source systems and LEDs in medical, surgical, dental and aesthetic practices' – available at: https://www.gov.uk/government/publications/guidance-on-the-safe-use-of-lasers-intense-light-source-systems-and-leds.

Problems with surgical instruments

4.56 If any problems are identified with instruments or sets of instruments, this should be referred to MHRA through the Yellow Card Scheme (https://yellowcard.mhra.gov.uk/).

Endoscopy

4.57 Annex F contains advice on the precautions to be taken for endoscopic procedures on patients with, or "at increased risk" of, CJD.

Ophthalmology

4.58 Annex L contains advice on the precautions to be taken for ophthalmic procedures on patients with, or "at increased risk" of, CJD.

Anaesthesia and intensive care

4.59 The Association of Anaesthetists of Great Britain and Ireland (AAGBI) in 2008 published an update to their guidance "Infection Control in Anaesthesia." This guidance includes a section on prion diseases and can be found here.

Community healthcare of CJD patients

4.60 People should not be dissuaded from routine contact with CJD patients as both CJD and vCJD are not thought to present a risk through normal social or routine clinical contact.

4.61 No special measures over and above standard infection prevention and control precautions are generally required for caring for CJD patients in the community, as it is unlikely that procedures will be adopted that will lead to contact with high or medium risk tissues.

Caring for symptomatic patients at home

4.62 Those caring for patients at home should be advised of the standard infection prevention and control practices that would apply to any patient. They should be provided with disposable gloves, paper towels, waste bags and sharps containers, as appropriate. Provision should be made with the Local Authority for the removal and disposal of clinical waste and sharps from the home.

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

Spillages

4.64 It is assumed that all spillages in the community will be of low risk material, for example blood and urine. Standard infection prevention and control precautions

should be followed to clear up spillages of material from patients with, or "at increased risk" of, CJD in the community. Spillages should be cleared up as quickly as possible, keeping contamination to a minimum. Disposable gloves and an apron should be worn when removing such spillages. The surface should then be washed thoroughly with detergent and warm water.

4.65 For spillages of large volumes of liquid, absorbent material should be used to absorb the spillage. A number of proprietary absorbent granules are available for such use, including those containing sodium dichloroisocyanurate, but it should be noted that these do not deactivate TSE agents.

4.66 Any waste (including cleaning tools such as mop heads, and PPE worn) should be disposed of as normal clinical waste.

Clinical waste

4.67 Clinical waste should be disposed of as set out in Table 4b.

Bed linen

4.68 Patients' clothes and bed linen can be washed as normal, although in the interests of general hygiene it may be preferable to wash fouled linen separately. Commercial laundry services can be used as an alternative and, particularly where patients are incontinent, a laundry service can be of great help to carers.

Pregnancy

4.69 In the event that a patient with, or "at increased risk" of, CJD becomes pregnant, no additional infection prevention and control precautions need to be taken during the pregnancy. 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 the procedures described in paragraph 4.39.

Dentistry

4.70 The risks of transmission of infection from dental instruments are thought to be very low provided satisfactory standards of infection prevention and control and decontamination are maintained. There is no reason why any patient with, or "at

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increased risk" of, CJD, should be refused routine dental treatment. Such people can be treated in the same way as any member of the general public.

4.71 Information for dentists about the management of patients with, or "at increased risk" of, CJD can be found in *Decontamination Health Technical Memorandum 01-05: Decontamination in primary care dental practices (March 2013)* at: https://www.gov.uk/government/publications/decontamination-in-primary-care-dental-practices. This also includes advice for dentists on the re-use of endodontic instruments and vCJD.

4.72 Dental instruments used on patients with, or "at increased risk" of, CJD can be handled in the same way as those used in any other low risk surgery, *i.e*. these instruments can be reprocessed according to best practice and returned to use. Dentists are reminded that any instruments labelled by manufacturers as 'single-use' should not be re-used under any circumstances.

4.73 Advice on the decontamination of dental instruments can be found in the Department of Health guidance HTM01-05 *Decontamination Health Technical Memorandum 01-05: Decontamination in primary care dental practices (March 2013)*. This guidance has been produced to reflect a reasonable and rational response to emerging evidence around the effectiveness of decontamination in primary care dental practices, and the possibility of prion transmission through protein contamination of dental instruments. It is available at: https://www.gov.uk/government/publications/decontamination-in-primary-care-dental-practices.

After death

4.74 Guidance on dealing with the bodies of patients with, or "at increased risk" of, CJD, is contained in Annex H. This includes advice on carrying out post mortem examinations and transportation of bodies, and advice for undertakers on embalming, funerals and cremations.

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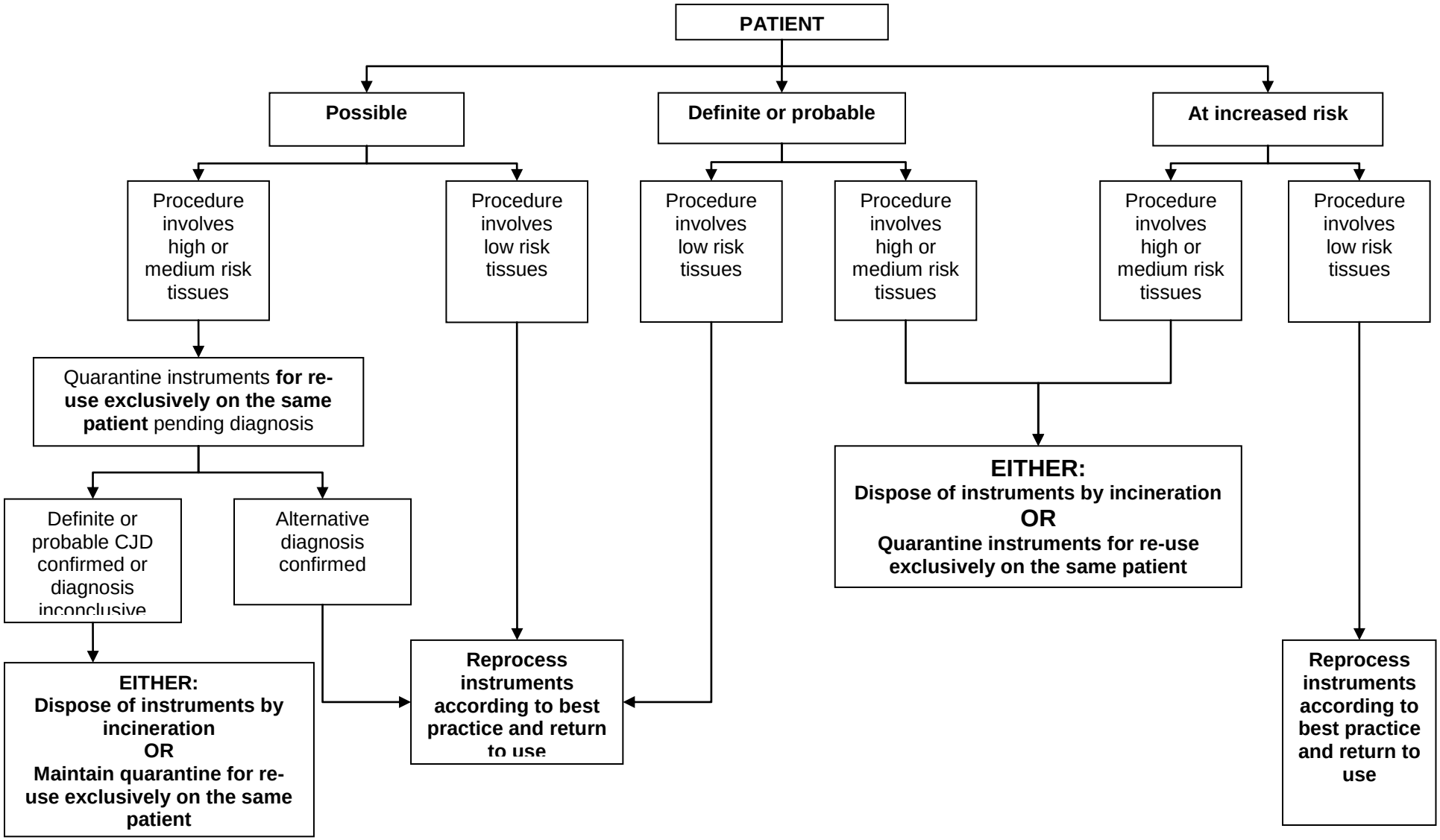
Algorithm chart for precautions for reusable instruments for surgical procedures on patients with, or "at increased risk" of, CJD, vCJD and other human prion diseases



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ANNEX A1

Distribution of TSE infectivity in human tissues and body fluids

A1.1 There is evidence that the distribution of the disease-specific partially protease-resistant form of prion protein (PrP^{TSE}) in tissues is more widespread in the body in variant CJD (vCJD) patients than in patients affected by sporadic CJD (1, 2, 3). In sporadic CJD, the presence of abnormal prion protein in patients with clinical disease appears to be restricted to the central nervous system (CNS). However, abnormal prion protein has been detected in various lymphoid tissues, including tonsils, spleen, gastrointestinal lymphoid tissue (appendix and rectum), lymph nodes, thymus and adrenal gland of patients with clinical vCJD. Abnormal prion protein has also been detected in lymphoid tissues within the appendix removed from 2 patients some 8 and 24 months before they developed vCJD (4, 5) suggesting that abnormal prion protein could be present in the lymphoid tissue of people incubating vCJD for some time before the onset of clinical disease. In similar tests, abnormal prion protein has not been detected in these tissues from sporadic CJD patients. Infectivity has been demonstrated in tonsil and spleen in vCJD by experimental transmission (6).

A1.2 PrP^{TSE} has been identified in posterior spinal nerve roots in only an occasional case of sporadic CJD and GSS (7), but not in peripheral nerve in vCJD (3, 8). Transmission studies on peripheral nerve samples from cases of sporadic CJD by intracerebral inoculation into primates have shown no evidence of infectivity (9). PrP^{TSE} has been detected in spinal dorsal root ganglia and trigeminal ganglia in vCJD (8), and in trigeminal ganglia in sporadic CJD (10). PrP^{TSE} has also been detected in olfactory epithelium in sporadic CJD patients at post mortem (11), and in the olfactory tract in vCJD (12). Infectivity and PrP^{TSE} have not been detected in dental pulp in a series of sporadic CJD cases (13), and PrP^{TSE} was not detected in the alveolar nerve, dental pulp, gingiva, salivary gland, tongue in a small series of vCJD cases (14).

A1.3 Table A1 presents current information on the distribution of infectivity in tissues and body fluids in CJD other than vCJD, and in vCJD, based on data from experimental studies, where available, and on information from other

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studies of natural TSE disease in humans and animals. It also shows where PrP^{TSE} has been detected in tissues.

A1.4 The precise relationship between the presence of PrP^{TSE} and infectivity is not certain – for example, the absence of detectable PrP^{TSE} does not necessarily mean absence of infectivity. Conversely, detection of small amounts of PrP^{TSE} in a tissue does not necessarily mean that it will transmit disease in all circumstances. This guidance has been formulated on the basis of likelihood of the presence of infectivity using the identification of PrP^{TSE} as a specific marker. In general terms, there is thought to be a broad correlation between PrP^{TSE} load in a given tissue and the likelihood that the given tissue might present a risk of infection. The relative levels of PrP^{TSE} in different tissues provide useful information for the assessment of relative risks of different procedures.

A1.5 In Table A1, tissue infectivity is classified as high, medium or low, on the basis of infectivity assays in experimental animals. Although such studies are limited in CJD and vCJD tissues, the preliminary data that are available support the findings in tissues from other natural and experimental TSE models. Therefore the relative levels of PrP^{TSE} in different tissues provide useful information for the assessment of relative risks of different surgical and endoscopic procedures.

A1.6 The information given in this Annex describes the position at the time of publication. This will be kept under review and is subject to change as further information becomes available.

Table A1 – Distribution of TSE infectivity in human tissues and body fluids

Key: **+ve** = tested positive **-ve** = tested negative
NT = not tested **P** = infectivity proven in experimental transmission studies

Tissue	Presence of abnormal prion protein and level of infectivity			
	CJD other than vCJD		vCJD	
	PrP^{TSE} detected	Assumed level of infectivity	PrP^{TSE} detected	Assumed level of infectivity
Brain	**+ve**	High **P**	**+ve**	High **P**

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Spinal cord	**+ve**	High **P**	**+ve**	High **P**
Cranial nerves, specifically the entire optic nerve and only the intracranial components of the other cranial nerves	**+ve**	High	**+ve**	High
Cranial ganglia	**+ve**	High	**+ve**	High **P**
Posterior eye, specifically the posterior hyaloid face, retina, retinal pigment epithelium, choroid, subretinal fluid, optic nerve	**+ve**	High **P**	**+ve**	High
Pituitary gland	**+ve**	High (?)	**+ve**	High (?)
Spinal ganglia[1]	**+ve**	Medium	**+ve**	Medium **P**
Olfactory epithelium	**+ve**	Medium	**NT**	Medium
Dura mater[2]	**-ve**	Low	**+ve**[4]	Low
Tonsil	**-ve**	Low	**+ve**	Medium **P**
Lymph nodes and other organised lymphoid tissues containing follicular structures	**-ve**	Low **P**	**+ve**	Medium **P**
Gut-associated lymphoid tissue	**-ve**	Low	**+ve**	Medium
Appendix	**-ve**	Low	**+ve**	Medium
Adrenal gland	**-ve**	Low	**+ve**	Medium
Spleen	**+ve**	Low **P**	**+ve**	Medium **P**
Thymus	**-ve**	Low	**+ve**	Medium
Anterior eye and cornea	**-ve**	Low	**-ve**	Low
Peripheral nerve	**+ve**	Low	**+ve**	Low
Skeletal muscle	**+ve**	Low	**+ve**	Low
Dental Pulp	**-ve**	Low	**-ve**	Low
Gingival Tissue	**NT**	Low	**-ve**	Low
Blood and bone marrow	**NT**	Low	**-ve**	Low
CSF[3]	**-ve**	Low **P**	**-ve**	Low
Placenta	**-ve**	Low	**-ve**	Low
Urine	**-ve**	Low	**-ve**	Low
Other tissues	**-ve**	Low **P**	**+ve**[4]	Low

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[1]Spinal ganglia have a high assumed level of infectivity in the WHO Guidelines. However, unpublished results on the infectivity of spinal ganglia indicate that this tissue is of medium infectivity.

[2]Dura mater is designated low infectivity as virtually no detectable abnormal prion protein has been found in cases of CJD; however, as grafts of these tissues are associated with CJD transmission, probably as a result of contamination by brain and because of the lengthy period of implantation in the CNS, procedures conducted on intradural tissues (i.e. brain , spinal cord and intracranial sections of cranial nerves) or procedures in which human dura mater was implanted in a patient prior to 1992, remain high risk.

[3]Although PrP^{TSE} has not been detected in the CSF in either sporadic or variant CJD (15), experimental transmission of infectivity has been achieved from CSF in sporadic CJD in 4 of 27 primates by intracerebral inoculation (9) indicating that levels of infectivity are likely to be much lower than in the central nervous system.

[4]PrPTSE has been detected in dura mater, skin, kidney, liver, pancreas, ovary and uterus in a case of vCJD in USA with a lengthy duration of illness (16). Earlier studies of these tissues in UK vCJD cases gave negative results (2,8,17).

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A comprehensive list of references is given in the WHO Guidelines which should be consulted when further detail is required:

WHO – Guidelines on tissue infectivity distribution in transmissible spongiform encephalopathies; updated 2010
http://www.who.int/bloodproducts/tablestissueinfectivity.pdf

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Annex A.2

Distribution of infectivity in animal tissue and body fluids

Introduction

A.2.1 The following table (Table A2) presents a guide to the possible presence of TSE infectivity in various tissues and body fluids of cattle (exposed naturally or experimentally and orally to first passage BSE agent), sheep and goats (exposed naturally to scrapie agents and potentially to the BSE agent) irrespective of the stage of incubation. Table A2 has been updated in June 2010 taking account of the updated WHO Guidelines published in 2010 (WHO, 2010).

A.2.2 This is the first time that the WHO Guidelines include tissues from Cervidae affected with Chronic Wasting Disease (CWD). CWD has not been reported in Europe despite some surveillance for it and there are no specific regulations in force. Should information on TSE infectivity in CWD be required, for example in regard to Cervidae in zoos or in animals in transit through our ports, please see updated 2010 WHO Guidelines.

A.2.3 Throughout this document the term PrP^{TSE} is used to denote the disease-specific, partially protease resistant form of PrP. In the previous version the term PrP-res was used but for practical purposes PrP^{TSE} and PrP-res are the same.

A.2.4 Additional notes are ascribed to certain entries to explain the differences (sometimes of interpretation) between the equivalent WHO table and Table A2, or to take account of new information. In case of doubt, please refer to the WHO Guidelines.

A.2.5 Specified risk material (SRM) from cattle, sheep and goats in the UK and most other EU Member States, as at February 2007, is listed in a new table – Table A3 in this document. Please refer to the FSA website for up-to-date information and definitions.

A.2.6 The list of tissues in Table A2 is divided into three categories;

- High infectivity tissues: Central nervous system (CNS) tissues and other tissues anatomically closely associated with them (in italics in the attached table). These become detectably infected in the later stages of all TSEs and into the clinical phase of disease.
- Lower infectivity tissues: A range of peripheral tissues including some or all (depending on species) lymphoreticular system (LRS) tissues that may be infected from shortly after exposure.
- Tissues that have either been bioassayed with no infectivity being detected, and/or tested for PrP^{TSE} and found negative.

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A.2.7 A fourth category of tissues has not been tested in any of the species and therefore must remain as of uncertain infectivity. However, no tissue in this category is likely to have high infectivity but could become cross-contaminated in certain circumstances.

A.2.8 The following notes are of considerable importance when the table data are used in risk assessments:

- The precise relationship between the presence of PrP^{TSE} and infectivity is not certain. For example, the absence of detectable PrP^{TSE} does not necessarily mean the absence of infectivity. Conversely, detection of small amounts of PrP^{TSE} in a tissue does not necessarily mean that it would transmit disease in all circumstances.
- No account has been taken of the fact that a tissue having no detectable infectivity could become contaminated by inadequate care being taken at the point of collection. Such contamination could be direct (from other infected tissues) or indirect (from contaminated instruments). Furthermore, certain methods of stunning animals (such as those involving penetration of the cranium or use of a pithing rod) prior to killing by bleeding out may cause infected brain emboli to be dispersed into the blood stream and thence also to the heart, lungs and possibly to other organs and tissues.
- In the EU and some other countries certain tissues of ruminant species are categorised as SRM on the basis of a judgment that in an infected animal they would be, or might be infected. The list of tissues classed as SRM may be varied depending on the geographical BSE risk (GBR) ascribed to the host country. Some tissues in the current EC SRM list may not have demonstrated either infectivity or PrP^{TSE}, nevertheless any requirements of the law must be followed.
- In research laboratories, tissues from every challenged animal potentially present a risk. However, in diagnostic laboratories in the UK, tissues listed in Table A.2 and the WHO table will present a risk less frequently unless they come from a suspect case of TSE or from a high-risk group.

A.2.9 Extensive data on the distribution of infectivity, additional information and references can be found in the WHO guidelines at the WHO website:

http://www.who.int/bloodproducts/tse/WHO%20TSE%20Guidelines%20FINAL-22%20JuneupdatedNL.pdf. The WHO tables have copious notes which are not included in this ANNEX so the WHO tables should be consulted to aid interpretation of the indicated result, in any case of doubt or to extend knowledge.

The 2010 WHO update can be found at:

http://www.who.int/bloodproducts/tablestissueinfectivity.pdf

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TABLE A2: Distribution of TSE infectivity in animal tissues and body fluids

	CATTLE		SHEEP AND GOATS	
TISSUE	**INFECTIVITY**	**PrP^{TSE}**	**INFECTIVITY**	**PrP^{TSE}**
HIGH INFECTIVITY				
Brain	+	+	+	+
Spinal ganglia (dorsal root ganglia)	+	+	+	+
Spinal cord	+	+	+	+
Trigeminal ganglia	+	+	NT	+
Retina	+	NT	NT	+
Optic nerve	+	NT	NT	+
Pituitary gland	-	NT	+	+
LOWER INFECTIVITY				
Peripheral nervous system				
Cauda equina	-	NT	NT	NT
Peripheral nerves	[+]	+	+	+
Autonomic ganglia	NT	+	NT	+
Lymphoreticular tissues				
Spleen	-	-	+	+
Lymph nodes	-	-	+	+
Nictitating Membrane	+	-	[+]	+
Thymus	-	NT	+	+
Tonsil	+	-	+	+
Alimentary tract				
Oesophagus	-	NT	[+]	+
Fore-stomachs	-	NT	[+]	+
Abomasum	-	NT	[+]	+
Duodenum	-	-	[+]	+

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Jejunum	-	+	[+]	+
Ileum	+	+	+	+
Colon/caecum	-	-	+	+
Rectum	NT	NT	NT	+
Reproductive tissues				
Placenta	-	NT	+	+
Ovary	-	NT	-	-
Uterus	-	NT	-	-
Body fluids, secretions and excretions				
CSF	-	NT	+	-
Blood	-	?	+	?
Saliva	NT	NT	-	NT
Milk	-	-	+	[+]
Urine	-	NT	-	-
Faeces	-	NT	-	NT
Other tissues**				
Adrenal	[+]	+	+	-
Liver	-	NT	+	-
Pancreas	-	NT	+	NT
Nasal mucosa	-	NT	+	+
Blood vessels	-	NT	NT	+
Skeletal Muscle*	[+]	NT	[+]	+
Salivary gland	-	NT	+	NT
Mammary gland/udder	-	NT	-	+
Skin	-	NT	-	+
Adipose tissue	-	NT	NT	NT
Heart/pericardium	-	NT	-	NT
Lung	-	NT	-	-
Kidney	-	-	[+]	+
Bone marrow	(+)	NT	+	NT
Tongue	-	NT	[+]	+

NO DETECTABLE INFECTIVITY

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Reproductive tissues				
Testis	-	NT	-	-
Prostate/Epididymis/				
Seminal vesicle	-	NT	-	-
Semen	-	NT	-	-
Placenta fluids	-	NT	NT	NT
Fetus	-	NT	-	-
Embryos	-	NT	?	NT
Musculo-skeletal tissues				
Bone	-	NT	NT	NT
Tendon	-	NT	NT	NT
Other tissues**				
Trachea	-	NT	NT	NT
Thyroid gland	NT	NT	-	NT
Body fluids, secretions and excretions**				
Colostrum	(-)	-	(?)	NT
Cord blood	-	NT	NT	NT

Key:

Italic type	Tissues included due to close anatomical proximity to high infectivity tissues
+	Positive transmission or presence of PrP^{TSE} detected
-	Bioassay negative or PrP^{TSE} not detected
NT	Bioassay not undertaken or PrP^{TSE} not tested for
NA	Not applicable
No detectable infectivity	Tissues not included in other parts of the table but bioassayed and /or tested for PrP^{TSE} with negative result.
( )	Limited or preliminary data
?	Uncertain interpretation
[]	Infectivity or PrP^{TSE} data based exclusively on bioassays in transgenic (Tg)mouse over-expressing the PrP-encoding gene, or PrP^{TSE} amplification methods

* In cattle, preliminary data indicate a low level of infectivity in the *M. semitendinosus* from one cow with clinical BSE. A homogenate of this muscle was inoculated i/c-i/p into ten highly BSE-sensitive transgenic mice and PrP^{TSE} was detected in one mouse (Buschmann and Groschup, 2005). No transmissions have been reported when various bovine tissues have been inoculated into either susceptible mice or cattle by the i/c-i/p or i/c routes respectively. Concern has been expressed about possible infectivity in lingual tonsillar

tissue at the root of the tongue, though the tongue itself shows no detectable infectivity (Wells *et al*., 2005).

** Some tissues tested in humans have not been tested in animals such as cornea, some dental tissues, sweat, tears, mucus and bile.

SPECIFIED RISK MATERIAL

A.2.10 Specified Risk material (SRM) includes those tissues of cattle, sheep and goats which are known to, or might potentially, harbour detectable BSE infectivity in infected animals. SRM is excluded from the human food and animal feed chains and cannot be used for any other purpose. The tissues which fall within the current definition of SRM are listed on the UK Food Standards Agency website http://www.food.gov.uk/safereating/animaldiseases/bse/what/beef/controls and are given below in Table A3.

TABLE A3 Specified risk material in the EU (as at November 2006)

Specified Risk Material in all Member States from 25 May 2006	
Cattle	**All ages** ▪ The tonsils, the intestines, from the duodenum to the rectum, and the mesentery **Over 12 months** ▪ Skull excluding the mandible but including the brains and eyes, and spinal cord **Over 24 months** ▪ Vertebral column, excluding the vertebrae of the tail the spinous and transverse processes of the cervical, thoracic and lumbar vertebrae, the median sacral crest and the wings of the sacrum, but including the dorsal root ganglia
Sheep and goats	**All ages** ▪ The spleen and the ileum **Over 12 months (or permanent incisor erupted)** ▪ Skull including the brains and eyes, tonsils, spinal cord

REFERENCES

A comprehensive list of references is given in the WHO Guidelines which should be consulted when further detail is required. The following are selected, relatively recent, publications of relevance to the Tables above.

General

WHO. *Guidelines on tissue infectivity distribution in transmissible spongiform encephalopathies;* June 2006.
http://www.who.int/bloodproducts/tse/WHO%20TSE%20Guidelines%20FINAL-22%20JuneupdatedNL.pdf

WHO. *Guidelines on tissue infectivity distribution in transmissible spongiform encephalopathies;* Updated 2010.

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http://www.who.int/bloodproducts/tablestissueinfectivity.pdf

Bovine Spongiform Encephalopathy

Buschmann A, Groschup MH. Highly BSE sensitive transgenic mice confirm essential restriction of infectivity to the nervous system in clinically diseased cattle. *J. Infect Dis* 2005; **192**:934-42

Everest SJ, Thorne LT, Hawthorn JA, Jenkins R, Hammersley C, Ramsay AM, Hawkins SA, Venables L, Flynn L, Sayers R, Kilpatrick J, Sach A, Hope J, Jackman R. No abnormal prion protein detected in the milk of cattle infected with the bovine spongiform encephalopathy agent. *J Gen Virol* 2006; **87**: 2433-2441

Hoffmann C, Ziegler U, Buschmann A, Weber A, Kupfer L, Oelschlegel A, Hammerschmidtand B, Groschup MH. Prions spread via the autonomic nervous system from the gut to the central nervous system in cattle incubating bovine spongiform encephalopathy. *J Gen Virol* 2007; **88**: 1048–55

Iwamaru Y, Okubo Y, Ikeda T, Hayashi H, Imamura M, Yokoyama T, Shinagawa M.
PrPSc distribution of a natural case of bovine spongiform encephalopathy. In: Kitamoto T, ed. *Prions. Food and Drug Safety*. Springer Verlag, New York, 2005

Wells GAH, Spiropoulos J, Hawkins SAC, Ryder SJ. Pathogenesis of experimental bovine spongiform encephalopathy (BSE): pre-clinical infectivity in tonsil and observations on lingual tonsil in slaughtered cattle. *Vet Rec* 2005; **156**: 401-7.

Scrapie

Andreoletti O, Lacroux C, Chabert A, Monnereau L, Tabouret G, Lantier F, Berthon P, Eyenne F, Lafond-Benestad S, Elsen J-M, Schelcher F. PrP(Sc) accumulation in placentas of ewes exposed to natural scrapie: influence of foetal *PrP* genotype and effect on ewe-to-lamb transmission. *J Gen Virol* 2002; **83**: 2607-16.

Casalone C, Corona C, Crescio MI, Martucci F, Mazza M, Ru G, Bozzetta E, Acutis PL, Caramelli M. Pathological prion protein in the tongues of sheep infected with naturally occurring scrapie. *J Virol* 2005; **79**: 5847-9.

Specified Risk Material

FSA (Food Standards Agency UK). List of tissues which fall within the current definition of Specified Risk Material. 2006:
http://www.food.gov.uk/safereating/animaldiseases/bse/what/beef/controls

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Annex B

Diagnostic criteria

B1. Paragraphs 4.17 and 4.18 in Part 4 of this guidance, including Table 4a**,** categorise CJD patients in descending order of risk, distinguishing between *symptomatic* and *asymptomatic* patients. *Symptomatic* patients are those who fulfil the internationally accepted diagnostic criteria, set out below, for *definite*, *probable* and *possible* CJD or vCJD (http://www.cjd.ed.ac.uk/criteria.htm).

B2. Suspect cases are classified according to these criteria by a neurologist from the National CJD Surveillance Unit (NCJDSU), on an on-going basis. The classification is recorded at 4 "key" stages:

- at notification;
- when the patient was first seen, in life, by a neurologist from the NCJDSU;
- the highest classification on the sole basis of clinical information (i.e. not including neuropathological information);
- when a NCJDSU review is completed (i.e. when the case-file is closed). The completed case file may, or may not, include neuropathological data

B3. The date of any change of classification and the reason for such a change is recorded as necessary in the NCJDSU.

Classification criteria

Sporadic CJD

B4. Neuropathological/immunocytochemical confirmation is required for a diagnosis of definite sporadic CJD.

B5. *Probable* sporadic CJD patients will have rapidly progressive dementia, **and at least two** of the following four symptoms:

a) myoclonus
b) visual or cerebellar problems
c) pyramidal or extrapyramidal features
d) akinetic mutism

plus typical electroencephalogram (EEG) with generalised triphasic periodic complexes at approximately 1 per second,

or clinical criteria for *possible* sporadic CJD (see below) **and** a positive assay for 14-3-3 protein in the cerebrospinal fluid (CSF).

B6. *Possible* sporadic CJD patients will have rapidly progressive dementia, **two** of the symptoms listed in paragraph B5(a)-(d) above **and** a duration of less than 2 years.

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Iatrogenic (accidentally transmitted) CJD

B7. *Definite* iatrogenic CJD requires a neuropathological diagnosis of CJD in a patient with a recognised risk factor for iatrogenic CJD (see Box B1).

Probable iatrogenic CJD is defined as either a progressive predominantly cerebellar syndrome in a human pituitary growth hormone recipient, **or** a clinical diagnosis of probable CJD (see definition in paragraph B5 above) in a patient with a recognised risk factor for iatrogenic CJD (see Box B1)

Box B1

RELEVANT EXPOSURE RISKS FOR THE CLASSIFICATION AS IATROGENIC CJD

The relevance of any exposure to disease causation must take into account the timing of the exposure in relation to disease onset

- Treatment with human pituitary growth hormone, human pituitary gonadotrophin or human dura mater graft
- Corneal graft in which the corneal donor has been classified as definite or probable human prion disease
- Exposure to neurosurgical instruments previously used in a case of definite or probable human prion disease
- Transfusion of blood from a donor subsequently diagnosed with vCJD

This list is provisional as previously unrecognised mechanisms of human prion disease may occur

Genetic TSE

B8. *Definite* genetic TSE requires a neuropathological confirmation of TSE, **plus either** *definite* TSE in a first degree relative (i.e. a parent, child or sibling), **or** a pathogenic prion protein gene (*PRNP*) mutation (see Box B2).

Probable genetic TSE is defined as a progressive neuropsychiatric disorder **plus** either *definite* or *probable* TSE in a first degree relative, **or** a pathogenic *PRNP* mutation (see Box B2).

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Box B2

***PRNP* MUTATIONS ASSOCIATED WITH GSS* NEUROPATHOLOGICAL PHENOTYPE**

P102L, P105L, A117V, G131V, F198S, D202N, Q212P, Q217R, M232T, 192 bpi

***PRNP* MUTATIONS ASSOCIATED WITH CJD NEUROPATHOLOGICAL PHENOTYPE**

D178N-129V, V180I, V180I+M232R, T183A, T188A, E196K, E200K, V203I, R208H, V210I, E211Q, M232R, 96 bpi, 120 bpi, 144 bpi, 168 bpi, 48 bp*del*

***PRNP* MUTATIONS ASSOCIATED WITH FFI** NEUROPATHOLOGICAL PHENOTYPE**

D178N-129M

***PRNP* MUTATION ASSOCIATED WITH VASCULAR PrP AMYLOID**

Y145s

***PRNP* MUTATIONS ASSOCIATED WITH PROVEN BUT UNCLASSIFIED PRION DISEASE**

H187R, 216 bpi

***PRNP* MUTATIONS ASSOCIATED WITH NEURO-PSYCHIATRIC DISORDER, BUT NOT PROVEN PRION DISEASE**

I138M, G142S, Q160S, T188K, M232R, 24 bpi, 48 bpi, 48 bpi + nucleotide substitution in other octapeptides

*GSS – Gertmann-Straussler-Scheinker disease
**FFI – Fatal Familial Insomnia

variant CJD (vCJD)

B9. *Definite* vCJD patients will have a progressive neuropsychiatric disorder **and** neuropathological confirmation of the disease, showing spongiform change and extensive PrP^{Sc} deposition with florid plaques throughout the cerebrum and cellebellum.

B10. *Probable* vCJD patients can be classified under two sets of criteria:

(I) They will have progressive neuropsychiatric disorder of a duration greater than 6 months, where routine investigations do not suggest an alternative diagnosis. They will also have **at least four** of the following five symptoms:

a) early psychiatric symptoms (depression, anxiety, apathy withdrawal, delusions)
b) persistent painful sensory symptoms (including both frank pain and/or unpleasant dysaesthesia)
c) ataxia
d) myoclonus or chorea or dystonia
e) dementia

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An EEG will not show the typical appearances of sporadic CJD, **or** no EEG has been performed and there is a symmetrical high signal in the posterior thalamus on a MRI brain scan ([1] Zeidler et al 2000).

These patients would have had no history of potential iatrogenic exposure and no evidence of a familial form of TSE.

(II) Alternatively, a *probable* vCJD patient will have had a progressive neuropsychiatric disorder for a period of longer than six months, where routine investigations do not support an alternative diagnosis, and where there is no history of potential of iatrogenic exposure or evidence of a familial form of TSE, **plus** a tonsil biopsy which is positive for PrP^{Sc}.

B11. *Possible* vCJD patients will have progressive neuropsychiatric disorder of a duration greater than 6 months, where routine investigations do not suggest an alternative diagnosis, and there is no history of potential iatrogenic exposure or evidence of a familial form of TSE. They will **also** have **at least four** out of five of the symptoms listed in paragraph B10 (I) (a)-(e) above **and** an EEG that does not show the typical appearance of sporadic CJD **or** no EEG has been performed.

Patients who do not fulfil the criteria for possible CJD

B12. The NCJDSU have designated three additional categories for patients who are referred to the Unit but who do not meet the criteria for *possible* CJD. These can be summarised as:

(i) **Diagnosis unclear** – the diagnostic criteria for *definite*, *probable* or *possible* CJD are not met, nor is there a reasonable alternative diagnosis. CJD therefore remains a possibility;

(ii) **CJD thought unlikely** – information indicates that a clinical diagnosis of CJD is very unlikely because of atypical disease features, and/or an atypical course, and/or atypical clinical investigation results, and/or a reasonable alternative diagnosis is made but is <u>not</u> confirmed. This category includes cases which recover clinically without a firm alternative diagnosis;

(iii) **definitely not CJD** – information indicates that CJD is <u>not</u> the diagnosis and there is an alternative definite diagnosis proven on the basis of clinical examination, clinical investigations or pathology.

[1] Zeidler M, Sellar RJ, Collie DA, Knight R, Stewart G, Macleod MA, Ironside JW, Cousens S, Colchester AC, Hadley DM, Will RG. The pulvinar sign on magnetic imaging in variant Creutzfeldt-Jakob Disease. Lancet. 2000; **355:** 1412-8

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ANNEX C

GENERAL PRINCIPLES OF DECONTAMINATION AND WASTE DISPOSAL

Summary of advice
Annex C provides information on the general principles of decontamination and waste disposal for transmissible spongiform encephalopathies (TSEs).

Previous revision date: November 2009
Changes new to this edition:

Date	Change	Notes
February 2015	Change of terminology from “infection control” to “infection prevention and control”.	Changed throughout the document as appropriate.
February 2015	Decontamination cycle diagram updated, to allow for new prion deactivation technologies.	This change affects paragraph C2.
February 2015	Addition of advice to clean instruments as soon as possible after use.	Paragraphs C4 and C5 have been added and the numbering of subsequent paragraphs changed accordingly.
February 2015	Clarification that the use of sodium hypochlorite is at ambient temperature.	This change affects paragraph C8.
February 2015	Additional advice on the use of formic acid.	This change affects paragraph C10.
February 2015	Expansion of the section on ‘Other processes’.	This change affects paragraph C17, and paragraphs C18-C20 have been added.
February 2015	Addition of a section on ‘Protein detection’.	Paragraphs C21-C23 have been added.
February 2015	Addition of a table with details of recent research projects relating to protein detection and decontamination, funded by the Department of Health.	Table C2 has been added.
February 2015	Update of the references to other relevant guidance.	These changes affect Table C3.

Introduction

C1. This annex provides information on the general principles of decontamination and waste disposal for transmissible spongiform encephalopathies (TSEs). A list of selected guidelines and standards related to decontamination and waste disposal is included as Table C3. Guidance on decontamination and waste disposal in a healthcare setting can be found in Part 4 of this guidance. Guidance on decontamination and waste disposal in a laboratory setting can be found in Part 3 of this guidance.

The Decontamination Cycle for reusable medical equipment

C2.

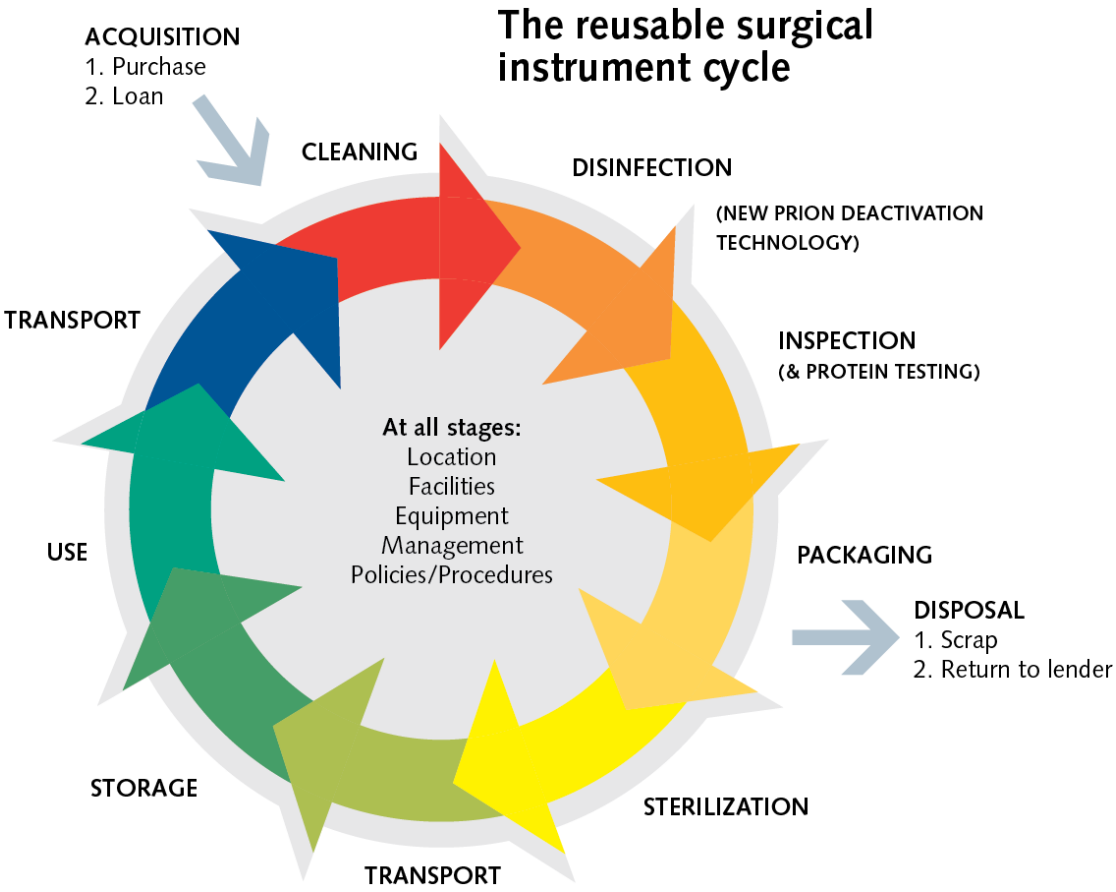

Diagram from Department of Health CFPP 01-01

Decontamination and TSE agents

C3. TSE agents are particularly resistant to standard physical and chemical methods of inactivation and decontamination. **Therefore, effective cleaning is of great importance in the removal of these agents.**

C4. Research demonstrates that allowing surgical instruments to dry for more than fifteen minutes before reprocessing greatly increases the amount of

residual protein contamination[1,2,3,4]. Therefore instruments should be transported to the sterile services department (SSD) immediately after the close of the procedure, for cleaning and reprocessing as soon as practically possible. This will make the cleaning process more effective, hence reducing the risks to the patients and staff handling the devices. If devices cannot be returned in a timely manner, it is important that the instruments are kept moist using appropriate methods approved and verified by the SSD.

C5. For endoscopes, the bedside clean should take place immediately after the procedure has been carried out, and it is recommended that the endoscopes should be manually cleaned according to the manufacturer's recommendations and passed through an Endoscope Washer Disinfector as soon as possible after use. See Annex F for further guidance about decontamination of endoscopes.

C6. Details of chemical and gaseous disinfectants and physical processes commonly used for decontamination, and their effectiveness at reducing infectivity, are outlined below. **It should be noted that combinations of some agents and/or processes could be effective, for example, physical/chemical combinations such as autoclaving with sodium hydroxide.**

Chemical decontamination

C7. **Most chemical disinfectants are ineffective at reducing infectivity and some, acting as protein fixatives, may stabilise the agent** (see Table C1).

Sodium hypochlorite

C8. Sodium hypochlorite is considered to be effective at reducing infectivity but only at concentrations (20,000ppm available chlorine for 1 hour at ambient temperature) that pose certain practical constraints. The following should be taken into account when considering the use of sodium hypochlorite:

- It must not be used on open surfaces *i.e.* benches due to the possible release of chlorine gas
- It corrodes metal and steel
- It is incompatible with formaldehyde, alcohols and acids
- It is rapidly inactivated by protein residues

[1] Lemmer *et al*. 2004. Decontamination of surgical instruments from prion proteins: in vitro studies on the detachment, destabilization and degradation of PrP^{Sc} bound to steel surfaces. *Journal of General Virology*, 85; 3805-3816.

[2] Rutala and Weber 2001. Creutzfeldt-Jakob disease: recommendations for disinfection and sterilization. *Clinical Infectious Diseases*, 32; 1348-1356.

[3] Lipscomb *et al*. 2007. Effect of drying time, ambient temperature and pre-soaks on prion-infected tissue contamination levels on surgical stainless steel: concerns over prolonged transportation of instruments from theatre to central sterile service departments. *Journal of Hospital Infection*, 65; 72-77.

[4] Secker *et al.* 2011. Adsorption of prion and tissue proteins to surgical stainless steel surfaces and the efficacy of decontamination following dry and wet storage conditions. *Journal of Hospital Infection*, 78; 251-255.

- Concentrated stock dilutions last for only approximately 2-3 weeks
- Diluted solutions are not stable and should be made up daily

Sodium hydroxide

C9. Sodium hydroxide (2M for 1 hour) has a substantial effect, and will reduce infectivity to an acceptable level when used at ambient temperature. An increase in temperature will increase effectiveness. The following should be taken into account when considering the use of 2M sodium hydroxide:

- It should not be used on aluminium or zinc
- It will not cause fumes but is damaging to body tissue
- It is an irritant and harmful as dust

Formic acid

C10. Formic acid (96% for 1 hour) may be used for histological samples of human or animal tissue that have previously been fixed in formalin. For material not treated with formic acid prior to processing, the immersion of formalin-fixed tissue sections (5µm or less) in undiluted formic acid (*i.e.* 96% or above) for at least 5 minutes is considered appropriate as a risk reduction measure. However, it should not be used on tissue that has previously been exposed to phenol, as this interacts deleteriously with formic acid.

Table C1: Ineffective chemical disinfectants

Chemical disinfectants commonly used for decontamination that are INEFFECTIVE at reducing infectivity
Alcohols[1]
Ammonia
ß-propiolactone
Chlorine dioxide
Ethylene oxide
Formaldehyde and related compounds[1]
Glutaraldehyde and related compounds[1] (e.g. orthophthalaldehyde [OPA])
Hydrochloric acid (Not reliably effective for practicable use)
Hydrogen peroxide
Iodophors
Peracetic acid
Aqueous solutions of phenol (≤10% phenol)
Sodium dichloroisocyanurate (e.g. 'Presept')[2]
10,000ppm sodium hypochlorite (Not reliably effective for practicable use)

[1]These agents are strong fixatives, may stabilise infectivity and thereby decrease the efficiency of the decontamination process

[2]The rate of release of chlorine from this product is insufficient to ensure complete inactivation of the agent

Phenol

C11. Phenol (≥ 90% phenol) is highly effective at eliminating infectivity. Phenol is a toxic, corrosive and irritant chemical which can be absorbed through mucous membranes, wounds and intact skin, and should be used cautiously and with the appropriate personal protective clothing.

Physical processes

Incineration

C12. Incineration is effective at removing the infectious agent and eliminating infectivity. Temperatures over 600ºC are likely to be practically effective, and 850ºC is commonly used in practice. Temperatures ≥1000 ºC can produce sterility. The particle size of material to be combusted should be suitably small to ensure efficient heat penetration to the centre.

Autoclaving

C13. Autoclaving remains an important method of reducing infectivity. Different strains of TSE are known to vary in their sensitivity to heat.

C14. The following methods will reduce infectivity but cannot be relied upon to completely eliminate infectivity (either porous load or gravity displacement).

- 121°C for 15 minutes
- 134-137°C for 3 minutes
- 134-137°C for 18 minutes
- Six successive cycles of 3 minutes

C15. The 'Prion Cycle' found on some benchtop vacuum autoclaves will also reduce infectivity **but will not eliminate infectivity entirely**. See MHRA Safety Notice 'SN 2002(11): Benchtop vacuum steam sterilizers – the 'prion cycle', available here.

Radiation

C16. Ionising, UV or microwave radiation at conventional doses are not effective at reducing infectivity.

Other processes

C17. A number of anti-prion technologies are in development. In 2008 the Engineering and Science Advisory Committee into the Decontamination of Surgical Instruments including Prion Removal (ESAC-Pr) produced a report on prion inactivating agents. This report provides advice on various anti-prion technologies then available or in development, their applicability to the current decontamination process for reusable medical equipment, and the direction of future research needs. The report can be accessed here.

C18. Many products developed for prion inactivation have only been available as a pre-soak. There are problems associated with the soaking of instruments, and the ESAC-Pr report specifically notes that:

"It is apparent that there needs to be greater discussion between the disinfectant product manufacturers, washer disinfector manufacturers and the end users,

particularly the Decontamination Leads and the Sterile Services Managers. The overwhelming conclusion of these professionals is that using these products, as a manual pre-soak is not a viable option in operating departments or in SSDs. It is not possible to validate reliably the soaking of instruments in open containers of chemical. Further, the question of penetration of chemical into serrations and box joints cannot be guaranteed. Therefore, it is vital that chemicals intended for this purpose are incorporated into the existing decontamination cycle practices i.e. as part of the washer disinfector process."

C19. A Working Group of the Advisory Committee on Dangerous Pathogens TSE Subgroup was convened in 2014 to assess the outputs of Department of Health funded research projects aimed at improving the evidence base for the decontamination of reusable surgical instruments and protein detection. The Working Group reviewed several novel technologies then in development for protein detection and decontamination. It is hoped that these technologies will make decontamination practices even more effective in the future.

C20. New technologies being developed need to reflect the operational requirements of the service. The Engineering Research Group has suggested that a routine test for washer disinfectors could be developed to measure the cleaning efficacy at validation and routine testing, such as daily or weekly tests. This method could be based on a process challenge device system that will monitor the optimised wash cycles; the results must be quantifiable and objective. This method should be sensitive to the requirements of this document and be able to deliver a consistent and accurate set of results that can be assessed by the unit management and Notified Bodies.

Protein detection

C21. Work commissioned by the Department of Health indicates the upper limit of acceptable protein contamination after processing is 5μg BSA equivalent per instrument side. A lower level is necessary for neurosurgical instruments.

C22. It is necessary to use protein detection methods to check for the efficient removal of protein from surgical instruments after processing. Protein levels are used as an indication of the amount of prion protein contamination. Ninhydrin swab kits are commonly used for this purpose, but recent evidence shows that ninhydrin is insensitive[5,6]. Furthermore, proteins are poorly desorbed from instruments by swabbing[6]. Other commonly used methods have also been shown to be insensitive[7].

[5] Lipscomb *et al.* 2006. The sensitivity of approved Ninhydrin and Biuret tests in the assessment of protein contamination on surgical steel as an aid to prevent iatrogenic prion transmission. *Journal of Hospital Infection*, 64; 288-292.

[6] Nayuni *et al.* 2013. Critical evaluation of ninhydrin for monitoring surgical instrument decontamination. *Journal of Hospital Infection,* 84, 97-102.

[7] Nayuni and Perrett 2013. A comparative study of methods for detecting residual protein on surgical instruments. *Medical Device Decontamination (incorporating the IDSc Journal),* 18, 16-20.

C23. New technologies are required on the market that can detect protein on instruments *in situ*, in nanogram quantities.

Table C2: Research projects relating to protein detection and decontamination recently funded by the Department of Health

Project	Topic	Publications arising to date
007/0194 Cold Gas Plasma Decontamination of Flexible Endoscopes	Novel technology for decontamination of endoscopes.	
007/0196 Endoscope Decontamination: defining the problem	Decontamination of endoscopes	Hervé, R.C. and Keevil, C.W. 2013. Current limitations about the cleaning of luminal endoscopes. *Journal of Hospital Infection* 83, 22-29.
007/0200 Optimisation of Automated Washer Disinfector Performance	Parameters contributing to optimised automated washer disinfector performance.	Nayuni, N. and Perrett, D. 2014. Valipro tags for the monitoring of washer disinfector efficiency. *Medical Device Decontamination (incorporating the IDSc Journal)* 18, 16-20.
007/0201 Meta and cluster analysis on Animal Models Used for TSE Decontamination Research	Literature review of animal models used in decontamination research.	
007/0202 Protein Detection Trial in SSDs	High sensitivity protein detection in SSD environments.	Perrett D and Nayuni N 2014. Assessing protein contamination on surgical and dental instruments Chapter 23 *in Decontamination in Hospitals and Healthcare*. Edited by Dr J.T. Walker, Woodhead Publishers Perrett D,*et al.* 2014. The *in-situ* detection of residual protein on surgical instruments: Development of the ProReveal system. *Medical Device Decontamination (incorporating the IDSc Journal)* 18, 8-17 Nayuni N, *et al.* 2013. A critical evaluation of ninhydrin as a protein detection method for monitoring surgical instrument decontamination in hospitals. *J Hospital Infection* 84, 97-102 Nayuni N. and Perrett D. 2013. A comparative study of methods for detecting residual protein on surgical instruments*. Medical Device Decontamination (incorporating the IDSc Journal)* 18, 16-20
007/0203 Protein Detection Trial	Detection of residual protein on instruments.	*Continued overleaf*

007/0204 Evaluation of EFSCAN Protein Detection for Monitoring Decontamination	Detection of residual protein on instruments.	Smith, A., *et al.* 2014. Dental handpiece contamination: a proteomics and surface analysis approach. *Biofouling*, 30, 29-39
007/0208 Selection and Preclinical Evaluation of Coatings for Surgical Instruments	Coating surgical instruments to minimise protein attachment.	

Table C3: Selected guidelines and standards related to decontamination and waste disposal

Name	Date published	Brief description
93/42/EEC The Medical Devices Directive	1993 UK law since 1998	This Directive under European Law covers the placing on the market and putting into service of Medical Devices (other than active implantable and *in vitro* diagnostic devices). Available here. Essential requirements in the Directive are listed under Annex 1. Two essential requirements under section 8 – Infection and microbial contamination – are particularly relevant: "8.4: Devices delivered in a sterile state must have been manufactured and sterilised by an appropriate validated method." "8.5: Devices intended to be sterilised must be manufactured in appropriately controlled (e.g. environmental) conditions."
Medical Devices Regulations	2002	These UK Regulations are drawn from the Medical Devices Directive 93/42/EEC
Department of Health NHS Estates and Facilities Policy (formerly NHS Estates) Health Building Notes (HBNs) HBNs provide advice to project teams designing and planning new buildings and adapting/extending existing buildings. HBNs are available at: https://www.gov.uk/government/collections/health-building-notes-core-elements		
Department of Health Estates and Facilities Policy (formerly NHS Estates) Engineering Health Technical Memoranda (HTM) and Choice Framework for local policy and procedures (CFPP) HTMs and CFPPs provide evidence-based policy and guidance on the management and decontamination of reusable medical devices and other aspects of decontamination in healthcare settings.		
CFPP 01-01 Management and decontamination of surgical instruments (medical devices) used in acute care	2013	This CFPP offers best practice guidance on the whole decontamination cycle including the management and decontamination of surgical instruments used in acute care. It is in four parts: Part A – Formulation of local policy and choices Part B – Common elements Part C – Steam sterilization Part D – Washer disinfectors Part E - Alternatives to steam for the sterilization of reusable medical devices https://www.gov.uk/government/publications/management-and-decontamination-of-surgical-instruments-used-in-acute-care
CFPP 01-04 Decontamination of linen for health and social care	2013	This CFPP amalgamates earlier versions of laundry guidance. Earlier documentation incorporated in and superseded by this guidance includes HSG(95)18 and parts of Health Building Note 25 – 'Laundry'. https://www.gov.uk/government/publications/decontamination-of-linen-for-health-and-social-care *Continued overleaf*

CFPP 01-06 Management and decontamination of flexible endoscopes	2013	This CFPP covers flexible endoscope management and decontamination. It is divided into five volumes: • Policy and management • Design and installation • Operational management • Validation and verification • Testing methods https://www.gov.uk/government/publications/management-and-decontamination-of-flexible-endoscopes
HTM 01-05 Dental Decontamination	2013	This guidance has been produced to reflect a reasonable and rational response to emerging evidence around the effectiveness of decontamination in primary care dental practices, and the possibility of prion transmission through protein contamination of dental instruments.https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/170689/HTM_01-05_2013.pdf
HTM 07-01 Safe management of healthcare waste	2013	This document is a best practice guide to the management of healthcare waste. Healthcare waste refers to any waste produced by, and as a consequence of, healthcare activities. For the purposes of this document, this guidance also applies to offensive/hygiene and infectious waste produced in the community from non-NHS healthcare. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/167976/HTM_07-01_Final.pdf
Technical requirements and Guidance in Scotland		
The Glennie framework	2001	This document specifies the requirements for sterile service provision across NHS Scotland. http://www.scotland.gov.uk/Publications/2001/10/10106/File-1
Compliant Dental Local Decontamination Units in Scotland (Primary Care)	2013	This document specifies the requirements for compliant reprocessing of dental devices in Local Decontamination Units (Primary Care). http://www.hfs.scot.nhs.uk/publications-1/decontamination/
Provision of Compliant Podiatry Instruments	2014	This document specifies the requirements for compliant provision of podiatry instruments. http://www.hfs.scot.nhs.uk/services/decontamination-services/guidance/
Other relevant decontamination guidance		http://www.hfs.scot.nhs.uk/services/decontamination-services/guidance/ *Continued overleaf*

Welsh Health Technical Memoranda (WHTMs) **http://www.wales.nhs.uk/sites3/page.cfm?orgid=254&pid=64101**		
WHTM 01-01 Decontamination of medical devices within acute services	2013-2014	This document gives guidance on the whole decontamination cycle in the management and decontamination of surgical instruments used in acute care. It is in five parts: Part A – Management and environment Part B – Common elements Part C – Steam sterilization and steam for sterilization Part D – Washer disinfectors Part E - Alternatives to steam for the sterilization of reusable medical devices
WHTM 01-05 Decontamination in primary care dental practices and community dental services	2014	This guidance relates to locally conducted decontamination in primary care dental services
WHTM 01-06 Decontamination of flexible endoscopes	2014	This guidance allows local decisions to be made in the formulation of an appropriately developed, risk controlled, operational environment within the healthcare facilities that decontaminate flexible endoscopes. It is in five parts: Part A - Policy and management Part B - Design and installation Part C - Operational management Part D - Testing methods Part E - Validation and verification
Guidance in Northern Ireland		
PEL (13) 12*: Choice Framework for Local Policies and Procedures (CFPP)01-01*	2013	Management and Decontamination of Surgical Instruments (Medical Devices) Used in Acute Care: Parts A, B,C,D, and E for use in Northern Ireland. http://www.dhsspsni.gov.uk/pel_13_12_part_1.pdf
PEL (13) 15: *Choice Framework for Local Policies and Procedures (CFPP)01-06*	2013	Reprocessing of Flexible Endoscopes: For use in Northern Ireland. http://www.dhsspsni.gov.uk/pel-13-15.pdf
PEL (13) 16: *Northern Ireland Addenda to Choice Framework for Local Policies and Procedures (CFPP) 01-01*	2013	Management and Decontamination of Surgical Instruments (Medical Devices) Used in Acute Care and CFPP 01-06: Reprocessing of Flexible Endoscopes. NI/CFPP/01, NI/CFPP/02 and NI/CFPP/03 : Testing Requirements. http://www.dhsspsni.gov.uk/pel-13-16.pdf
HSS(MD)4/01	2001	Protocol for local decontamination of surgical instruments
HSS(MD)4/01	2001	Decontamination of reusable medical devices Addendum 3

Continued overleaf

HSS(MD)16/99	1999	Controls Assurance in Infection Control: Decontamination of Medical Devices. (and accompanying Decontamination Guidance CD-ROM)
HSS(MD)12/2007	2007	Decontamination of Surgical Instruments in light of National Institute for Health and Clinical Excellence (NICE) Guidance – Patient Safety and Reduction of Risk of Transmission of CreutzfeldtJakob Disease (CJ) via Interventional Procedures
PEL (13) 13	2013	Updated Northern Ireland Guidance on Decontamination in Primary Care Dental Practices: Health Technical Memorandum 01:05 2013 Edition http://www.dhsspsni.gov.uk/pel_13_13.pdf
Other relevant guidance		
Standards and Practice	2012	The Institute of Decontamination Sciences (IDSc), formerly the Institute of Sterile Services Management, has produced a revised third edition of this guidance, which sets out in detail the operational, technical and managerial requirements of decontamination services and provides a useful resource for anyone working in or around decontamination. The revised 3rd edition has been extensively updated to include the latest legislative framework referencing the work of the Healthcare Commission, ISO 13485 and the revised HBN13. A hardcopy of 'Standards and Practice' is free to full members of the Institute. Non-members can purchase hardcopies of the guidance. More information available at http://www.idsc-uk.co.uk/publications.php
Standards and Recommendations for Safe Perioperative Practice	2015	The Association for Perioperative Practice (AfPP), formally NATN, has produced the fourth edition of their perioperative standards and recommendations. The Decontamination Section is found within chapter 6 providing direction and guidance on all aspects of the decontamination life cycle processes, including direct links to all UK regions, National and International standards. The book is available to purchase via AfPP's website (www.afpp.org.uk/books-journals/afpppublication)

ANNEX D

TRANSPORT OF TSE INFECTED MATERIAL

CONTENTS and INDEX

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For legislation concerning transport of dangerous goods within, to or from Northern Ireland, see Appendix 2 for contact details for enquiries.

Legislative Background

International and national carriage of dangerous goods

D1. The **international carriage** of dangerous goods by road, rail, sea and air is explained in full at the Department for Transport's website: http://www.dft.gov.uk/pgr/freight/dgt1/overview/international/internationaltransport Importation of TSE-infected material by air or sea to the UK may involve customs forms and import permits for individual countries outside Europe.

D2. This document outlines the regulations and stipulations for **national carriage** of dangerous goods by road, rail, sea and air. However, as will be clear from the information below, many of these national regulations are derived from the international regulations for the carriage of dangerous goods, and thus the same rules apply for classification, packaging, marking and transporting.

National carriage by sea

D3. The safe transport of dangerous goods by sea in the UK, and internationally, is set out in the International Maritime Dangerous Goods (IMDG) Code.

D4. The carriage of dangerous goods by inland waterway in the UK is subject to the Dangerous Substances in Harbour Areas Regulations 1987 or British Waterways by-laws. The amount of dangerous goods moved by this mode within the UK is small. Most estuarial waterways are open to sea-going vessels and are therefore governed by the International Maritime Dangerous Goods (IMDG) Code.

D5. The carriage, loading, unloading and storage of dangerous goods in harbour areas in the UK is controlled by the Dangerous Substances in Harbour Areas Regulations 1987. Provisions are made under the Merchant Shipping Acts for ships' crews by way of the Merchant Shipping (Dangerous Goods and Marine Pollutants) Regulations 1997 which bring in the IMDG Code for domestic transport.

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National carriage by air

D6. Requirements for the carriage of dangerous goods in the UK, and internationally, by air are set out by the International Civil Aviation Organisation (ICAO) in the ICAO Technical Instructions for Safe Transport of Dangerous Goods by Air, which are revised every two years. The Air Navigation (Dangerous Goods) Regulations 2002, and subsequent amendment regulations, bring the ICAO Technical Instructions into domestic legislation.

National carriage by road and rail

D7. Carriage of dangerous goods by road and rail within Great Britain is required to comply with the European agreement concerning the international carriage of dangerous goods by road (ADR) and the Regulations concerning the international carriage of dangerous goods by rail (RID) subject to agreed derogations, exemptions etc. as set out in the Carriage of Dangerous Goods and Use of Transportable Pressure Equipment Regulations 2007, which came into force on 1st July 2007. Note that these are expected to be replaced by updated regulations in July 2009. ADR and RID are in turn based on the UN Recommendations on the Transport of Dangerous Goods (Model Regulations).

D8. For enquiries on legislation concerning transport of dangerous goods by road or rail in Northern Ireland – see Appendix 2 for contact details.

Application of relevant legislation

Transporting TSE infected material by road, rail and air in Great Britain

D9. There are 4 steps involved in the safe transport of TSE infected material by road, rail and air in Great Britain. These are:

(i) Classification of the samples to be transported

(ii) Packaging

(iii) Marking

(iv) Transporting

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Classification

D10. All TSE infected specimens of human and animal origin are classified for transport purposes as Dangerous Goods, in Class 6.2 Infectious Substances. The UN Model Regulations define infectious substances as: *"substances known or reasonably expected to contain pathogens*" and pathogens are defined as micro-organisms including (bacteria, viruses, rickettsiae, parasites, fungi) and other agents such as TSEs which can cause disease in humans or animals. Class 6.2 covers biological products used for diagnosis or research, genetically modified micro-organisms (GMMs), genetically modified organisms (GMOs), and clinical/biological waste. Determination of which UN number to assign within Class 6.2 Infectious Substances is based on whether the materials meet the criteria for a Category A or a Category B.

Category A

D11. An infectious substance which is carried in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease in otherwise healthy humans or animals and should be assigned to Category A, UN2814 (humans) or UN2900 (animals).

D12. Specimens would be assigned to Category A for transport if the source patient or animal has or may have a serious human or animal disease which can be readily transmitted from one individual to another, directly or indirectly, and for which effective treatment and preventive measures are not usually available.
Note: An exposure occurs when an infectious substance is released outside of the protective packaging resulting in physical contact with humans or animals.

D13. **TSE samples are not considered to be Category A for transport** as TSEs are not considered to be readily transmissible.

Category B

D14. An infectious substance which does not meet the criteria for Category A, and does not appear on the indicative list for Category A, should be assigned to Category B and UN 3373.

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TSE samples are considered to be Category B for transport, and thus transport of all TSE samples must follow the requirements of UN 3373.

D15. Category B substances, which are assigned to UN 3373, should be deemed to include specimens of human or animal material, including but not limited to, excreta, secreta, blood and its components, tissue and tissue fluid swabs and body parts, being transported for purposes such as research, diagnosis, investigational activities, disease treatment or prevention, but excluding live infected animals.

All TSE material including brain/spinal cord tissue and body fluid samples such as CSF, blood, urine and faeces must be sent as UN3373 Category B.

D16. Cell lines known to be infected with a TSE agent are considered biological agents under the Control of Substances Hazardous to Health Regulations (CoSHH), so should be transported as dangerous goods.

Packaging

D17. Category B specimens of TSE assigned to UN3373 must be packed in accordance with ADR packing instruction 650 for road and rail transport, and ICAO packing instruction P650 for airfreight (the ICAO packing instructions are also shown in the IATA Dangerous Goods Regulations). For full packaging details, particularly if transporting refrigerated or frozen specimens using ice, dry ice or liquid nitrogen, packaging instruction 650 should be consulted. Details of this packaging instruction are included in the Department for Transport's guidance document on transport of infectious substances.

D18. Packaging for Category B substances is not required to be UN-type approved, however it must meet all the requirements of P650 and the Department for Transport guidance document (as above). A P650 consists of a triple layer packaging system, comprising a primary receptacle, secondary packaging and outer packaging. For airfreight, the outer packaging must be rigid; for road and rail transport either the secondary or outer packaging must be rigid. The packaging supplier MUST provide clear instructions on filling and closing the package.

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D19. There are no weight limits on the quantity of Category B material contained within either the primary receptacle(s) or the total package for transport by road or rail. This is in contrast to transport by air where other than for body parts, organs or whole bodies the outer package must not contain more than 4kg

- On both passenger and cargo aircraft there is a 4L/4kg limit per outer package, with a IL limit per primary receptacle for liquids, whereas for solids the primary receptacle must not exceed the outer packaging mass limit of 4kg
- A whole organ such as brain is regarded as an exceptional consignment and as such the restriction of the weight of material that can be placed in the primary does not apply.

D20. It is permissible to have mixtures of samples within the same outer packaging providing each individual sample meets its specific requirements under packaging instruction 650.

Marking/Labelling

D21. Packaging must be clearly labelled with the delivery address and sender's details. The UN Number MUST be used with the proper shipping name which is "BIOLOGICAL SUBSTANCE CATEGORY B" in text that is at least 6mm high The text 'UN3373' must be placed in a diamond-shaped mark. The length of the line shall be at least 50mm, the width of the line shall be at least 2mm and the lettering shall be at least 6mm high.

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D22. TSE samples being sent as Category B substances must be marked and labelled as follows:

1. ”UN 3373 BIOLOGICAL SUBSTANCE CATEGORY B”
2. Name and full address of both shipper and consignee
3. Name and telephone number of the person responsible for the shipment (emergency contact)
4. In addition, the following labels must be placed on the overpack for shipments involving solid carbon dioxide (dry ice):
   - Hazard label for solid carbon dioxide (dry ice)
   - Net weight of dry ice
   - The overpack must be marked as “OVERPACK”

Transporting

D23. Consignors should always discuss the transport requirements with their chosen carrier.

D24. In general, samples that are travelling as UN3373 Biological substance Category B can be sent via the postal service (UK only) or using a courier. A dangerous goods document is not required for the transport of a Category B substance going by road or rail within Great Britain, or on an international RID/ADR journey within Europe. A copy of the emergency response procedure (see paragraph D27 below for an example of this), details of the sample enclosed, and a packing list must be provided with any package.

D25. If you are intending to import or export human body parts and tissue for non-therapeutic purposes then the guidance outlined in “The import and export of human body parts and tissue for non-therapeutic purposes Code of Practice” should be followed.

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D26. **Example emergency response sheet for TSE-infected material**

- Dangerous goods are infectious substances affecting humans Class 6.2, UN number 3373
- No immediate hazard to health unless ingested or injected into the body
- No risk of fire or explosion
- In event of accident wear disposable gloves and other necessary personal protective clothing for handling the material
- For spillages, cover areas with 2M sodium hydroxide or sodium hypochlorite (20,000ppm available chlorine). Note that both sodium hydroxide and sodium hypochlorite are caustic chemicals that may produce dangerous fumes. Appropriate personal protective clothing must be worn by handlers of these chemicals
- Use absorbent material to clean up the spillage
- Dispose of waste by incineration

Training

D27. All personnel involved in the transport of infectious substances should be given the appropriate training.

Transport of animals

D28. Exposure to agents in intact large animals, whether alive or dead, can be considered to be remote.

D29. Regulations covering the transport of live animals infected with a TSE agent are the responsibility of the Home Office and Defra in England, and the devolved administrations in Scotland and Wales (see Appendix 1). For information on transport of live animals within, to or from Northern Ireland, see Appendix 2 for contact details for enquiries.

Transport of livestock

D30. Farm livestock, particularly adult cattle, but also sheep and pigs, pose no significant risks from exposure to TSEs for the stockman, haulier or anyone else

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involved in livestock transport. There are, however, considerable physical risks to these occupations due to the unpredictable behaviour of large animals especially when they are moved to unfamiliar surroundings (see HSE Guidance on Handling and Housing Cattle). Livestock must be transported in accordance with animal welfare and animal identification legislation. Transport of animals exhibiting clinical signs of TSE is inadvisable.

D31. Although the incidence of Bovine Spongiform Encephalopathy (BSE) in the national herd is rapidly diminishing, TSE research with infected livestock is still ongoing and scrapie cases are routinely transported. If you need to transport clinical TSE cases then further guidance can be obtained from Animal Health (see Appendix 2 for contact details). *(Note: a special licence is required under the Animals (Scientific Procedures) Act 1986 for all experimental work on animals).*

D32. One exception to the remote risk of exposure to BSE when transporting cattle is where an animal has been orally dosed with BSE (or other TSEs) for experimental purposes. This procedure results in a risk of the agent being voided from the gut. A precautionary 28-day risk period has been agreed, and thus livestock that have been orally dosed within the last 28 days must not be transported. Where exceptional circumstances prevail, advice should be sought from HSE (see Appendix 2 for contact details).

Transport of small live animals

D33. Small live animals such as mice infected with TSE agents could pose a greater threat to humans than larger animals because of the risk from exposure to bites and scratches. There are unlikely to be many situations when infected small animals would need to be transported; however, in cases where there is no alternative then advice should be sought from HSE (see contacts information in Appendix 2) and the following adhered to:

- A thorough risk assessment must be carried out, which assesses:
    i. the time in transit
    ii. the infective agent
    iii. the number of animals

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iv. supervision by experienced staff
v. emergency procedures

- Animals must be transported in secure containers that protect the handler from the animals. The animals themselves can be considered to be the primary containment
- Containers must be fitted with suitable filters
- Animals must **not** be transported when there is a possibility of infectivity from the inoculum being shed in excrement and/or urine

D34. In addition the following regulations should be considered:

- The Animals (Scientific Procedures) Act 1986;
- The Welfare of Animals (Transport) (England) Order 2006 (SI 2006/3260)
- The Welfare of Animals (Transport) (Wales) Order 2007 (WSI 2007/1047(W.105))
- The Welfare of Animals (Transport) (Scotland) Regulations 2006 (SSI 2006/606)
- The Transmissible Spongiform Encephalopathy (England) Regulations 2008 (SI 2008/1881)
- The Transmissible Spongiform Encephalopathies (Wales) Regulations 2006 (WSI 2006/1226 (W.117)
- The Transmissible Spongiform Encephalopathies (Scotland) Regulations 2006 (SSI 2006/530)

Also see legislation on animal identification.

Transport of dead animals

D35. The Animal By-Products Regulations (ABPR) 2005 (parallel legislation in Scotland and Wales) lay down rules for the collection, transport and disposal of animal by-products. Animal by-products are defined as entire bodies or parts of animals or products of animal origin referred to in Article 4, 5 and 6 of Regulation (EC) No.1774/2002 not intended for human consumption, including ova, embryos and semen.

D36. **Dead animals infected with TSEs, and any TSE-infected tissue of animal origin, must be transported in accordance with ABPR 2005.**

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D37. Intact, dead, large animals do not pose a significant risk of transmitting TSE to humans. The animal itself can be considered to be the primary containment. In the TSE context, TSE infectivity will not be aerosolised, excreted, secreted or otherwise liberated from the central nervous system (CNS).

D38. Methods of killing which involve penetrating the cranial cavity should not be used for animals suspected of being affected with a TSE, as there is a risk of leakage of CSF fluid and possibly macerated neural tissue. The use of injectable barbiturates is the preferred method of euthanasia in such cases. If there is no alternative and a method of killing which involves penetrating the cranial cavity is used, the hole should be stoppered with an appropriately designed plug and the head enclosed in two layers of robust plastic sacks tied off at the neck of the animal.

D39. Only hauliers who have the necessary competences, training and appreciation of the risks involved should transport livestock and carcasses. Hauliers need to comply with the following:

Vehicles and containers must be leak proof and:

- Cleaned, washed and disinfected after each use
- Maintained in a clean condition
- Clean and dry before use
- Reusable containers must be dedicated to the carriage of a particular product to the extent necessary to avoid cross contamination
- Packaging must be incinerated or disposed of after use in accordance with instructions from the competent authority

D40. Bovine heads and whole brains must be double bagged, tied, and placed in robust plastic boxes (e.g. ‘Arca System’ boxes) before being transported by courier.

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ANNEX D – APPENDIX 1

Links to regulations, legislation and guidance

United Nations recommendations

- UN recommendations on the Transport of Dangerous Goods Model Regulations
  http://www.unece.org/trans/danger/publi/unrec/rev13/13files_e.html

International agreements and regulations on the transport of dangerous goods

- European agreement concerning the International Carriage of Dangerous Goods by Road (ADR) 2007 edition.
  http://www.unece.org/trans/danger/publi/adr/adr2007/07ContentsE.html

- Regulations concerning the International Carriage of Dangerous Goods by Rail (RID), Appendix C to the Convention Concerning International Carriage by Rail, 2007 edition. ISBN 10: 8086206289.

- International Maritime Dangerous Goods (IMDG) Code
  http://www.imo.org/Safety/mainframe.asp?topic_id=158

- ICAO Technical Instructions for Safe Transport of Dangerous Goods by Air, 2007-2008 edition
  http://www.icao.int/anb/FLS/DangerousGoods/TechnicalInstructions/

National regulations for the transport of dangerous goods

- Dangerous Substances in Harbour Areas Regulations 1987
  http://www.opsi.gov.uk/si/si1987/Uksi_19870037_en_1.htm

- Merchant Shipping (Dangerous Goods and Marine Pollutants) Regulations 1997
  http://www.opsi.gov.uk/si/si1997/19972367.htm

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- The Carriage of Dangerous Goods and use of Transportable Pressure Equipment Regulations 2007
  http://www.opsi.gov.uk/si/si2007/uksi_20071573_en_1
  Note that these are expected to be replaced by updated regulations in July 2009

- Air Navigation (Dangerous Goods) Regulations 2002
  http://www.opsi.gov.uk/si/si2002/20022786.htm

Other regulations

- The Animal By-Products Regulations (ABPR) 2005 (parallel legislation in Scotland and Wales) http://www.opsi.gov.uk/si/si2005/20052347.htm and http://www.defra.gov.uk/Animalh/by-prods/default.htm

- The Animals (Scientific Procedures) Act 1986
  http://www.archive.official-documents.co.uk/document/hoc/321/321-xa.htm

- The Welfare of Animals (Transport) (England) Order 2006 (SI 2006/3260)
  http://www.opsi.gov.uk/SI/si2006/20063260.htm

- The Welfare of Animals (Transport) (Wales) Order 2007 (WSI 2007/1047(W.105))
  http://www.opsi.gov.uk/legislation/wales/wsi2007/wsi_20071047_en_1

- The Welfare of Animals (Transport) (Scotland) Regulations 2006 (SSI 2006/606)
  http://www.opsi.gov.uk/legislation/scotland/ssi2006/20060606.htm

- The Transmissible Spongiform Encephalopathy (England) Regulations 2008 (SI 2008/1881)
  http://www.opsi.gov.uk/si/si2008/pdf/uksi_20081881_en.pdf

- The Transmissible Spongiform Encephalopathies (Wales) Regulations 2006 (WSI 2006/1226 (W.117)
  http://www.opsi.gov.uk/legislation/wales/wsi2006/20061226e.htm

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- The Transmissible Spongiform Encephalopathies (Scotland) Regulations 2006 (SSI 2006/530)
  http://www.opsi.gov.uk/legislation/scotland/ssi2006/20060530.htm

- The Control of Substances Hazardous to Health Regulations 2002
  http://www.opsi.gov.uk/SI/si2002/20022677.htm

Relevant guidance

- Department for Transport guidance on international transport of dangerous goods
  http://www.dft.gov.uk/pgr/freight/dgt1/overview/domestic/nationaltransport

- Department for Transport guidance on national transport of dangerous goods
  http://www.dft.gov.uk/pgr/freight/dgt1/overview/international/internationaltransport

- Department for Transport guidance on transport of infectious substances
  http://www.dft.gov.uk/pgr/freight/dgt1/guidance/guidancenonclass7/guidanceontransportofinfecti3186

- Carriage of Dangerous Goods Manual – HSE
  http://www.hse.gov.uk/cdg/manual/index.htm

- Biological agents: Managing the risks in laboratories and healthcare premises. Advisory Committee on Dangerous Pathogens.
  http://www.hse.gov.uk/biosafety/biologagents.pdf

- Defra guidance on Animal Welfare During Transport Requirements
  http://www.defra.gov.uk/animalh/welfare/farmed/transport.htm

- Defra guidance on Animal Identification Requirements
  http://www.defra.gov.uk/animalh/id-move/index.htm

- Defra guidance on Animal By-Products Requirements
  http://www.defra.gov.uk/animalh/by-prods/default.htm

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- Guidance on Handling and Housing Cattle
  http://www.hse.gov.uk/pubns/ais35.pdf

- BSE Occupational Guidance
  http://www.hse.gov.uk/pubns/web22.pdf

- Royal Mail Advice
  http://www.royalmail.com/portal/rm/jump2?catId=400023&mediaId=400044

- The import and export of human body parts and tissues for non-therapeutic uses. Department of Health Publications
  http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4009963

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ANNEX D – APPENDIX 2

Contact details

- **Department for Transport Dangerous Goods Division**
  Email: dgenquiries@vca.gov.uk
  Telephone: 01372 226111

- **For information on transportation within, to and from Northern Ireland:**
  Mr William Burns
  Health and Safety Inspector
  Health and Safety for Northern Ireland
  83 Ladas Drive
  Belfast
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  BT6 9FR
  Telephone: 0289 0546903
  Email: William.burns@detini.gov.uk

- **For advice on animal health and welfare:**

http://www.defra.gov.uk/animalhealth/about-us/contact-us/animal-health-offices.htm

- **For general advice, contact HSE:**
  Website: www.hse.gov.uk
  Email: hse.infoline@natbrit.com

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ANNEX E

Quarantining of surgical instruments

E1. Part 4 and Annex L of this guidance allows for the quarantining of instruments that have been used for procedures involving tissues designated as high or medium infectivity, on patients either;

- with, or at increased risk of, CJD/vCJD, for reuse exclusively on the same patient; or
- with a possible CJD/vCJD diagnosis, pending a confirmed diagnosis.

Although it is not expected that this facility will need to be used widely, this Annex provides guidance on the procedures which should be followed when quarantining surgical instruments may be considered.

E2. During a surgical procedure as defined in paragraph E1, instruments should be separated according to the principles set out in the NICE interventional procedures guidance 196. Instruments that come into contact with tissues designated as high or medium infectivity should be kept separate from those that only come into contact with tissues designated as low infectivity.

E3. After completion of a surgical procedure as defined in paragraph E1, single-use instruments should be separated and disposed of by incineration with normal clinical waste. Re-usable instruments that have only come into contact with tissues designated as low infectivity may be decontaminated and returned to routine use.

E4. Re-usable instruments that have come into contact with tissues designated as high or medium infectivity should be washed to remove gross soil. Care should be taken to avoid splashing and generating aerosols, by holding instruments below the surface of the water in a sink into which water is running and draining out continuously, for example in a sink in the theatre sluice room. Instruments should not be held directly under a flowing tap as this is likely to generate splashes. Operatives should wear protective gloves and either a visor or goggles, and care must be taken to avoid penetrating injuries. The sink does not require high level

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decontamination afterwards – the dilution effect from the running water will be sufficient to remove contamination.

E5. After washing, instruments should be placed on a disposable instrument tray and allowed to air-dry. They should then be placed in an impervious rigid plastic container with a close-fitting lid. The lid should be sealed with heavy duty tape and labelled with the patient's identification details (*i.e.* name, date of birth and hospital number). The label should also state the surgical procedure in which the instruments were used and the name of the responsible person (*e.g*. the Team or Unit Manager). The disposable instrument tray should be disposed of by incineration with normal clinical waste. The sealed box can be stored indefinitely in a suitable designated place until the outcome of any further investigations is known (see paragraph E6), or the instruments are required for another surgery on the same patient (see paragraphs E7 and E8).

E6. For patients with a possible CJD/vCJD diagnosis, if the patient is confirmed as suffering from CJD or vCJD, the box and its contents should be incinerated, or retained for use in research (see Part 4 for details), without any further examination. If an alternative diagnosis is confirmed, the instruments may be removed from the box by the responsible person (or a named deputy) and reprocessed according to best practice and returned to use. Additional decontamination procedures are not required.

E7. Rarely, it may be necessary to consider the re-use of a quarantined set of surgical instruments on the same patient. One such scenario would be the need to repeat a liver transplant on a patient who is at increased risk of vCJD. In these circumstances, the instrument set should be reprocessed through the Sterile Services Department in the usual manner. No special precautions are necessary because of the high dilution factor involved in the washer/disinfection process. It is important to ensure that the set is tracked through the whole decontamination cycle as previously directed.

E8. **Under no circumstances should quarantined instrument sets be reprocessed for use on other patients unless the diagnosis of CJD or vCJD has been**

positively excluded. The possibility of residual abnormal prion on the instruments is of far greater concern than the possibility of contamination of instruments in other sets processed in the washer/disinfector either concurrently or subsequently.

E9. Records must be kept of all decisions, and the Sterile Service Department must be informed about the decision before the instruments are sent for routine reprocessing.

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Annex F

ENDOSCOPY

Summary of advice

Annex F provides the definitive UK guidance on decontamination of flexible endoscopes for TSE infection prevention and control.

The specific recommendations in this guidance are complementary to national guidance on all aspects of endoscope decontamination such as Choice Framework for local Policy and Procedures 01-06 (CFPP 01-06)[i] and the British Society of Gastroenterology (BSG) Guidance on Decontamination of Equipment for Gastrointestinal Endoscopy[ii].

Annex F provides specific advice for the management of instruments used in all types of endoscopic procedures. This advice differs depending on the type of CJD that a patient has been diagnosed with, or for which symptoms are being investigated, and for those who are asymptomatic but for whom an increased risk of developing disease has been identified. It is important to note that the risks from CJD and vCJD are different, as the distribution of infectivity in tissues and body fluids differs (see Annex A1)

Paragraphs F4 to F27 set out the guidance for each circumstance in detail, while summary advice is provided in table F1 and table F2a.

Endoscopes currently in quarantine

Advice is given below regarding endoscopes that have been held in quarantine following previous use on patients who are “at increased risk” of vCJD.

Endoscopes that have been placed into quarantine on or after 1 January 2010, assuming not used to treat one of the patient categories described at paragraphs F21 to F24 should be reviewed as follows:

1) Was the endoscope properly decontaminated using a validated process prior to quarantine?

2) Is there tracking to demonstrate (1)?

3) Has the endoscope been stored properly whilst in quarantine (in a drying cabinet or at least positioned vertically, not coiled up in a case)?

If all the above are met, the endoscope can be returned to use. If the endoscope has been out of use for more than a few months it is recommended that it is returned to the manufacturer for service and a check of handling characteristics before returning to use.

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Previous revision date: February 2015
Changes new to this edition:

Date	Change	Notes
October 2015	Correction to a statement from the introductory section covering "Endoscopes currently in quarantine"	None

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F1. The general procedures set out in the ***Choice Framework for local Policy and Procedures 01-06 – Decontamination of flexible endoscopes: Policy and Management (CFPP 01-06)***[i] or equivalent national guidance and the ***BSG Guidance on Decontamination of Equipment for Gastrointestinal Endoscopy***[ii] (2014) should be followed. In order to decrease the risk of transmission of TSEs through endoscopic procedures, additional precautions for the decontamination of flexible endoscopes used in all patients with definite, probable or possible CJD/vCJD, and in those identified as "at increased risk" of developing CJD/vCJD, are recommended and general precautions are reinforced in this Annex:

(a) Channel cleaning brushes and, if biopsy forceps or other accessories have been passed, the rubber valve on the endoscope biopsy/instrument channel port should be disposed of as clinical waste after each use. Single use (*i.e.* disposable) biopsy forceps should be used routinely in all patients. This guidance endorses the advice of the BSG that endoscope accessories should be single use wherever possible. It is essential to have systems in place that enable endoscopes, together with all their detachable components and any re-used accessories, to be traced to the patients on whom they have been used.

(b) As defined below, endoscopes used for certain procedures in the CNS and nasal cavity in individuals with possible sporadic CJD, or in whom the diagnosis is unclear[iii], should be removed from use or quarantined pending diagnosis or exclusion of CJD (see Table F1 for clarity of this issue). The principles and procedures recommended for quarantining of surgical instruments in Annex E of this guidance should be followed, except the endoscope should be fully cleaned and decontaminated immediately after use, before being quarantined.

(c) Endoscopes other than those used in the CNS and nasal cavity, which have been used for invasive procedures in most individuals[iv] designated as "at increased risk" of vCJD, can be decontaminated to the standards set out in *CFPP 01-06* or equivalent national guidance and the *BSG guidance* and returned to use (see Table F2a). The endoscope should be put through all the normal stages of cleaning, and be disinfected separately from other equipment within an automated Endoscope Washer Disinfector (EWD).

(d) Aldehyde disinfectants with fixative qualities (such as glutaraldehyde and OPA) tend to stabilise rather than inactivate prions, and are no longer recommended for use in the UK. Non-fixative disinfectants are used instead.

(e) When decontaminating endoscope cleaning equipment, the EWD should be put through an "empty" self-disinfection cycle as per recommended routine. Provided that the cleaning

[i] CFPP 01-06 was published in June 2012 by the Department of Health and can be accessed via https://www.gov.uk/government/publications/management-and-decontamination-of-flexible-endoscopes

[ii] BSG Guidance on Decontamination of Equipment for Gastrointestinal Endoscopy (2014) at http://www.bsg.org.uk/clinical-guidelines/endoscopy/guidelines-for-decontamination-of-equipment-for-gastrointestinal-endoscopy.html

[iii] Patients with neurological disease of unknown aetiology who do not fit the criteria for possible CJD but where a diagnosis of CJD is being actively considered (see Annex B of this guidance)

[iv] This excludes a small number of asymptomatic individuals "at increased risk" of vCJD because they have received blood from a donor who later developed vCJD. Endoscopes used to treat these patients should be removed from use or quarantined to be re-used exclusively on the same individual. See Table F2a.

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equipment is decontaminated as indicated, there is no known risk of transmission of TSE agents via this route.

(f) Following use in patients at risk of vCJD endoscopic accessories (including normally reusable devices such as heater probes) and cleaning aids such as brushes should be disposed of by incineration.

F2. The bedside clean should take place immediately after the procedure has been carried out, and it is recommended that the endoscopes should be manually cleaned according to the manufacturers' recommendations, and passed through an EWD as soon as possible after use and in any case no more than 48 hours after the end of the procedure.

F3. PrP^{res} has been detected in the olfactory epithelium, but not the respiratory epithelium, of sporadic CJD patients (see paragraph 4.5 of Part 4 of this guidance). The olfactory epithelium is normally located along the roof of the nasal cavity but its distribution varies between individuals. On the lateral wall it may extend inferiorly onto the superior turbinate and the anterior insertion of the middle turbinate; on the medial wall it may extend onto the uppermost part of the septum. The advice of the consultant carrying out the endoscopic procedure in the nasal cavity should be sought to determine whether a risk of contamination of the endoscope with olfactory epithelium can be excluded with confidence. If such contamination cannot be excluded, precautions should be taken appropriate for medium infectivity tissues.

Definitions

F4. The definitions of different types of patients are as set out in:
paragraphs 4.17– 4.18 and Table 4a in Part 4; and
Annex B of this guidance.

Sporadic and other non-variant CJD

This includes sporadic CJD, sporadic fatal insomnia, VPSPr, iatrogenic CJD (other than iatrogenically acquired variant CJD), and genetic CJD, FFI and GSS.

Symptomatic sCJD patients (definite, probable)

F5. Neurological endoscopes would not normally be used on patients whose diagnosis is definite or probable sCJD. However, should such use be necessary, the endoscope should be single use if possible. If this is not feasible or appropriate, the endoscope should be removed from use or destroyed.

F6. Endoscopes that come into contact with the nasal cavity may, on occasion, be used in patients with definite or probable sCJD. If there is a risk that the endoscope could become contaminated with olfactory epithelium (see paragraph F2 above), a single use endoscope should be used if possible. If this is inappropriate, the endoscope should be removed from use or destroyed (as above).

F7. For all other types of endoscopy, decontaminate according to *CFPP 01-06* or equivalent national guidance and the *BSG guidance* with the additional precautions for flexible endoscopes as set out in paragraph F1 above.

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Symptomatic patients (possible sporadic, or diagnosis unclear, but variant CJD is **not** being considered)

F8. Neurological endoscopes would not normally be used on patients whose diagnosis is possible CJD or for whom the diagnosis of CJD is unclear. However, should use be necessary, a single use endoscope should be used if possible. If this is not appropriate, the re-usable endoscope should be quarantined pending a more definitive diagnosis. The quarantined endoscope may be re-used exclusively on the same individual patient if required. If further clarification of the diagnosis is not possible, the endoscope should be removed from use.

F9. Endoscopes that are used in the nasal cavity may, on occasion, be used in patients with definite or possible CJD. If there is a risk that the endoscope could become contaminated with olfactory epithelium (see paragraph F2 above), a single use endoscope should be used where possible. If this is not appropriate, the endoscope should be decontaminated singly as at F1(c-f), then quarantined pending a more definitive diagnosis. The quarantined endoscope may be re-used exclusively on the same individual (index) patient if required. If further clarification of the diagnosis is not possible, the endoscope should either be removed from use or retained for sole use on the index patient.

F10. For all other types of endoscopy, decontaminate according to *CFPP 01-06* or equivalent national guidance and the *BSG guidance*, with the additional precautions for flexible endoscopes as set out in paragraph F1 above.

Asymptomatic patients "at increased risk" of CJD (other than variant CJD)

F11. No special precautions are required for the use, in patients "at increased risk" of CJD, of rigid endoscopes without lumens that can be autoclaved. The guidance in Part 4 of this guidance for all surgical instruments can be followed.

F12. For other types of endoscope that are used for central nervous tissue investigations, single-use instruments should be used if possible. Where this is not possible without compromising clinical standards, the endoscope should be removed from use. Alternatively the endoscope can be decontaminated singly, as at F1(c-f) then quarantined after use to be re-used exclusively on the same individual patient if required.

F13. If there is a risk that an endoscope used in the nasal cavity could become contaminated with olfactory epithelium (see paragraph F2 above), a single use endoscope should be used where possible. If this is not appropriate, the endoscope should be removed from use. Alternatively the endoscope can be quarantined after use to be re-used exclusively on the same individual patient if required. For some procedures, the endoscope may be protected from contamination by a disposable sheath, which should then be destroyed by incineration. However, this does not obviate the need for routine decontamination following use on a patient. Additionally, in practice, it may be difficult to ensure effective protection, and advice should be sought from the surgical staff carrying out the procedure and the manufacturer of the endoscope to determine the practicality of this option.

F14. For all other types of endoscopy, decontaminate according to *CFPP 01-06* or equivalent national guidance and the *BSG guidance.*

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Variant CJD & CJD type uncertain

Symptomatic vCJD patients (definite, probable)

F15. Neurological endoscopes would not normally be used on patients whose diagnosis is definite or probable vCJD. However, should such use be necessary, the endoscope should be single use if possible. If this is not feasible or appropriate, the endoscope should be removed from use.

F16. Endoscopes that come into contact with the nasal cavity may, on occasion, be used in patients with definite or probable vCJD. If there is a risk that the endoscope could become contaminated with olfactory epithelium (see paragraph F2 above), a single use endoscope should be used if possible. If this is inappropriate, the endoscope should be removed from use.

F17. For all other types of endoscopy, providing decontamination of the endoscope is to approved standards, the use of the instrument for inspection in the absence of an invasive procedure, as defined in Table F2b, is deemed to be of low risk. If biopsy or another invasive procedure is carried out, the possibility of contamination of the instrument channel with lymphoid tissue means the endoscope should be decontaminated singly as at F1(c-f), then quarantined pending assessment of likely contact with potentially infected tissue.

Symptoms consistent with vCJD (possible or unclear diagnosis[v])

F18. Neurological endoscopes would not normally be used on patients whose diagnosis is possible vCJD or for whom the diagnosis of vCJD is unclear. However, should such use be necessary, a single use endoscope should be used if possible or the endoscope should be decontaminated singly as at F1(c-f), then quarantined pending a more definitive diagnosis. The quarantined endoscope may be re-used exclusively on the same individual (index) patient if required. If further clarification of the diagnosis is not possible, the endoscope should either be removed from use or retained for sole use on the index patient.

F19. Endoscopes that are used in the nasal cavity may, on occasion, be used in vCJD patients, and there is a risk that the endoscope could be contaminated with infectivity from the olfactory epithelium. Single use instruments should be used where possible. If this is not feasible or appropriate, the endoscope should be decontaminated singly as at F1(c-f), then quarantined pending confirmation of the diagnosis. The quarantined endoscope may be re-used exclusively on the same individual (index) patient if required. If further clarification of the diagnosis is not possible, the endoscope should either be removed from use or retained for sole use on the index patient.

F20. For all other types of endoscopy, providing decontamination of the endoscope is to approved standards, the use of the instrument for inspection in the absence of invasive procedures as defined in Table F2b, is deemed to be a low risk procedure. If an invasive procedure is carried out, the possibility of contamination of the instrument channel with

[v] Patients with neurological disease of unknown aetiology who do not fit the criteria for possible vCJD but where a diagnosis of vCJD is being actively considered (see Annex B of this guidance)

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lymphoid tissue means the endoscope should be decontaminated singly as at F1(c-f), then quarantined pending assessment of likely contact with potentially infected tissue. If this is considered possible and an alternative diagnosis is not obtained, the endoscope should be removed from use.

Asymptomatic patients "at increased risk" through receipt of labile blood components (whole blood, red cells, white cells or platelets) from a donor who later developed vCJD[vi]

F21. No special precautions are required for the use, of rigid endoscopes without lumens that can be autoclaved. The guidance in Part 4 of this guidance for all surgical instruments can be followed.

F22. Endoscopes that are used for central nervous tissue investigations may, on occasion, be used on patients "at increased risk" of developing vCJD and there is a risk that the endoscope could be contaminated with infectivity from the nerve tissue. Single use instruments should be employed if possible. Where this is not possible, the endoscope should be removed from use. Alternatively the endoscope can be decontaminated singly as at F1(c-f), then quarantined after use to be re-used exclusively on the same individual patient if required.

F23. If there is a risk that an endoscope used in the nasal cavity could become contaminated with olfactory epithelium (see paragraph F2 above), a single use endoscope should be employed where possible. If this is not feasible or appropriate, the endoscope should be removed from use. Alternatively the endoscope can be decontaminated singly as at F1(c-f)), then quarantined after use to be re-used exclusively on the same individual (index) patient if required. If further clarification of the diagnosis is not possible, the endoscope should either be removed from use or retained for sole use on the index patient.

F24. For all other types of endoscopy, providing decontamination of the endoscope is to approved standards, the use of the instrument for inspection in the absence of an invasive procedure, as defined in Table F2b, is deemed to be a low risk procedure. If an invasive procedure is carried out, the possibility of contamination of the instrument channel with lymphoid tissue means the endoscope should be decontaminated singly as at F1(c-f), then quarantined pending assessment of likely contact with potentially infected tissue. If this is considered possible the endoscope should be removed from use. For some procedures, it may be possible to shield the working channel of the endoscope from contamination by a disposable sheath. Once the procedure is completed, the tip of the accessory (e.g. biopsy forceps) is withdrawn into the sheath, before the tip of the sheath is cut off and, like the remainder of the sheath, is later destroyed by incineration.

All other asymptomatic patients "at increased risk" of vCJD

F25. No special precautions are required for the use, in all other patients "at increased risk" of vCJD, of rigid endoscopes without lumens that can be autoclaved. The guidance in Part 4 of this guidance for all surgical instruments can be followed.

[vi] These individuals may be identified at pre-surgical assessment - using Annex J in conjunction with Part 4 of this guidance.

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F26. Endoscopes that are used for central nervous tissue investigations may, on occasion, be used on patients "at increased risk" of developing vCJD and there is a risk that the endoscope could be contaminated with infectivity from the nerve tissue. Single use instruments should be employed if possible. Where this is not possible, the endoscope should be removed from use. Alternatively the endoscope can be decontaminated singly as at F1(c-f), and quarantined thereafter to be re-used exclusively on the same individual patient if required.

F27. If there is a risk that an endoscope used in the nasal cavity could become contaminated with olfactory epithelium (see paragraph F2 above), a single use endoscope should be employed where possible. If this is not feasible or appropriate, the endoscope should be removed from use. Alternatively the endoscope can be decontaminated singly as at F1(c-f)), then quarantined after use to be re-used exclusively on the same individual (index) patient if required. If further clarification of the diagnosis is not possible, the endoscope should either be removed from use or retained for sole use on the index patient.

F278. For all other types of endoscopy, decontaminate according to *CFPP 01-06* or equivalent national guidance and the *BSG guidance*, with the additional precautions for flexible endoscopes as set out in paragraph F1 above.

Currently funded research

F29. Recent research funded by the Department of Health highlights the problems and limitations associated with the cleaning of endoscopes[vii]. The research centres on the build up of biofilms and protein deposits in the lumen of endoscopes as a result of abrasion and wearing through routine use and the use of forceps and other instruments inserted through the working channel of the instrument. It suggests that micro organisms can be displaced and spread through the cleaning process.

F30. Research into the efficiency of decontamination of endoscopes including manual cleaning processes is ongoing. Currently all endoscopes should be decontaminated according to *CFPP 01-06* or equivalent national guidance and the *BSG guidance*, with the additional precautions for flexible endoscopes as set out in paragraph F1 above, and this should be reflected in the local policy.

[vii] Hervé and Keevil 2013. Current limitations about the cleaning of luminal endoscopes. *Journal of Hospital Infection*, 83; 22-29

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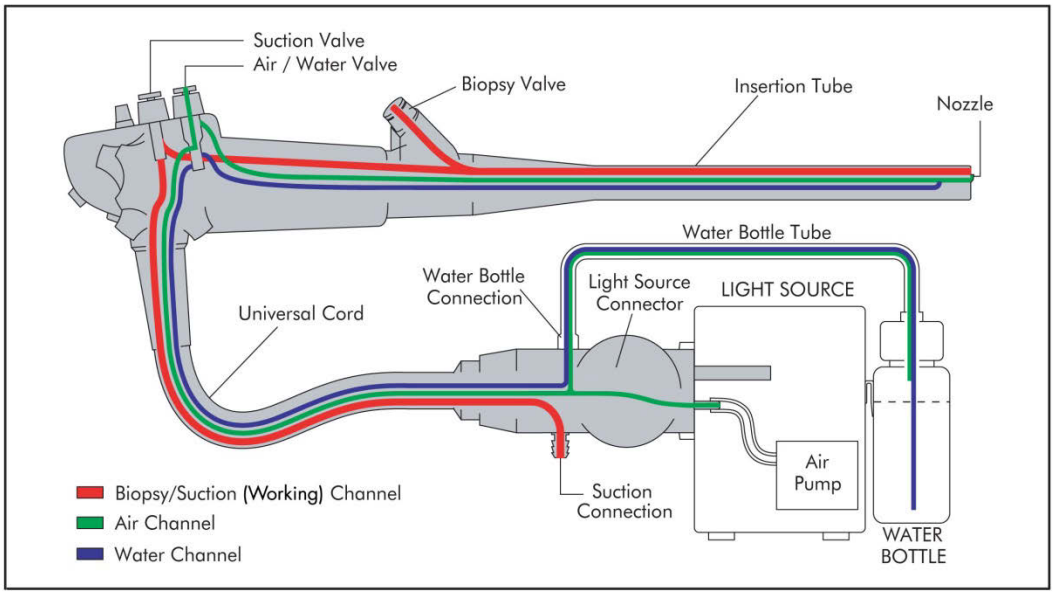
Definition of the working channel of an endoscope

F31 . The working channel of an endoscope is illustrated in the diagram below in red.



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SUMMARY OF PRECAUTIONS ADVISED FOR THE USE OF ENDOSCOPES

Table F1 CJD - other than vCJD

Tissue Infectivity	Status of patient		
	Symptomatic		Asymptomatic
	Definite/ probable	Possible / diagnosis unclear[1]	At risk[2] inherited/ iatrogenic
High: • Brain • Spinal cord	single use OR destroy after use OR quarantine[3] for re-use exclusively on the same index patient	single use OR quarantine pending diagnosis	single use OR destroy after use OR quarantine[3] for re-use exclusively on the same index patient
Medium: • Olfactory epithelium*	single use OR destroy after use OR quarantine[3] for re-use exclusively on the same index patient	single use OR quarantine pending diagnosis	single use OR destroy after use OR quarantine[3] for re-use exclusively on the same index patient
Low/none detectable: • All other tissues	no special precautions[4]	no special precautions[4]	no special precautions[4]

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Table F2a. vCJD and CJD type uncertain

Tissue Infectivity	Status of patient			
	Symptomatic		Asymptomatic	
	Definite /probable	**Possible vCJD, possible sCJD or diagnosis unclear[1]**	**At risk (blood[***] recipient from a donor who later developed vCJD)**	**At risk[2] Other iatrogenic**
High: • Brain • Spinal cord	single use OR destroy after use OR quarantine[3] for re-use exclusively on the same index patient	single use OR quarantine pending diagnosis	single use OR destroy after use OR quarantine[3] for re-use exclusively on same patient	single use OR destroy after use OR quarantine[3] for re-use exclusively on same patient
Medium: • Olfactory epithelium*	single use OR remove from use OR quarantine[3] for re-use exclusively on the same index patient	single use OR quarantine pending diagnosis	single use OR destroy after use OR quarantine[3] for re-use exclusively on the same index patient	no special precautions unless contaminated with olfactory epithelium* If contaminated: single use OR destroy after use OR quarantine[3] for re-use exclusively on the same index patient
Medium: Lymphoid tissue**	single use OR remove from use OR quarantine[3] for re-use exclusively on the same index patient	single use OR quarantine pending diagnosis	single use OR destroy after use OR quarantine[3] for re-use exclusively on the same index patient	no special precautions[4]
Low/none detectable: • All other tissues	no special precautions[4]	no special precautions[4]	no special precautions[4]	no special precautions[4]

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Notes

* The advice of the consultant carrying out the endoscopic procedure in the nasal cavity should be sought to determine whether a risk of contamination of the endoscope with olfactory epithelium can be excluded with confidence. If such contamination cannot be excluded, take precautions appropriate for medium infectivity tissues.

**For the purposes of this Annex, lymphoid tissue refers to the spleen, thymus, tonsils and adenoids, lymph nodes, the appendix and the gastro-intestinal tract sub-mucosa.

***A small number of individuals are known to have received labile blood components (whole blood, red cells, white cells or platelets) from a donor who later developed vCJD.

[1] This includes patients with neurological disease of unknown aetiology who do not fit the criteria for possible CJD but where a diagnosis of CJD is being actively considered (see also Annex B of this guidance).

[2] This advice refers to the use of flexible endoscopes in patients at risk of developing CJD. For guidance on the use of rigid endoscopes that can be autoclaved, refer to the guidance for the use of all surgical instruments in at risk patients in Part 4 of this guidance.

[3] Quarantined endoscopes may be re-used exclusively on the same individual patient if required. The principles behind the procedures recommended for quarantining of surgical instruments in Annex E of this Guidance should be followed except the endoscope should be fully cleaned and decontaminated immediately after use, before being quarantined. The endoscope should be decontaminated alone using an Automatic Endoscope Washer Disinfector (EWD). The EWD should be decontaminated as per paragraph F1(e) of this guidance.

[4] The decontamination procedures advised in paragraph F1 of this guidance, taken together with the ***CFPP 01-06*** or equivalent national guidance and ***BSG Guidance for Decontamination of Equipment for Gastrointestinal Endoscopy*** (2014) should be followed (http://www.bsg.org.uk/clinical-guidelines/endoscopy/guidelines-for-decontamination-of-equipment-for-gastrointestinal-endoscopy.html).

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Table F2b. Common flexible endoscopic procedures classified as invasive or non-invasive. (vCJD and CJD type uncertain).

The term "working channel" applies to the endoscope channel that is used for both the passage of accessories and the suction removal of liquids and gases.

	Procedure	Contamination of working channel	Mechanism	Invasive (+) or Non-Invasive (–)	Notes/ Exceptions
1	**ARTHROSCOPY, BRONCHOSCOPY AND CYSTOSCOPY**				
1a	All arthroscopy procedures	These procedures will not involve contact of the endoscope with infectious tissue.	None	–	
1b	Diagnostic cystoscopy or * bronchoscopy	Providing no biopsy is taken it is very unlikely that the endoscope will become contaminated*.	None. Tissue contamination would not result from a straightforward diagnostic procedure.	–	
1c	Cystoscopy with biopsy to obtain fixed lymphoid tissue	When a biopsy is taken of lymphoid tissue, there is a risk that the working channel could become contaminated with potentially infectious tissue.	Lymphoid tissue could come into contact with the lining of the working channel. Tissue may be deposited in the working channel.	+	Biopsy of the bladder can be considered non-invasive (-) if it can be determined with confidence that there has been no contact with, or invasion of, lymphoid tissue.
1d	Bronchoscopy with biopsy to obtain fixed lymphoid tissue	When a biopsy is taken of lymphoid tissue, there is a risk that the working channel could become contaminated with potentially infectious tissue.	Lymphoid tissue could come into contact with the lining of the working channel. Tissue may be deposited in the working channel.	+	Bronchoscopy with biopsy can be considered non-invasive (-) if it can be determined with confidence that there has been no contact with, or invasion of, lymphoid tissue.

Table F2b published: November 2005
revised and updated: June 2008

1e	Transbronchial biopsy	There is a risk that the working channel may become contaminated with lymphoid tissue during transbronchial biopsy.	Lymphoid tissue could come into contact with the lining of the working channel. Tissue may be deposited in the working channel.	**+**	
2	**ENDOSCOPIC ULTRASOUND (EUS)**				
2a	Diagnostic EUS	Providing no biopsy is taken it is very unlikely that the endoscope will become contaminated.	None. Tissue contamination would not result from a straightforward diagnostic ultrasound procedure.	**–**	
2b	EUS with biopsy	Biopsy utilises a needle that may result in contamination of the working channel with lymphoid tissue.	The needle is sheathed and therefore not in contact with working channel	**–**	
3	**UPPER GI ENDOSCOPY**				
3a	* Diagnostic gastroscopy	Providing no biopsy is taken it is very unlikely that the endoscope will become contaminated*.	None. Tissue contamination would not result from a straightforward diagnostic endoscopy.	**–**	

Table F2b published: November 2005
revised and updated: June 2008

3b	Gastroscopy with biopsy	Even with efficient single use forceps contamination of the working channel with submucosal lymphoid tissue is likely.	Contaminated tissue may come into contact with the lining of the endoscope working channel. Tissue may be deposited on the internal surface of the working channel. Decontamination not proven to remove the infective agent.	**+** (but see exception, right)	Cytology is of negligible risk provided a sheathed technique is used. Alternatively cytology (using a sheathed cytology device) could be taken at the first gastroscopy if malignancy is strongly suspected. Some larger channel endoscopes allow the passage of a sheath through which biopsy may be done while protecting the endoscope working channel from tissue contamination. Following biopsy, the tip of the biopsy forceps is fully retracted into the sheath, the tip of which is kept protruding from the endoscope tip throughout. The practice of taking a single biopsy and removing the endoscope with the forceps protruding, and then severing it with wire cutters, is to be discouraged.

Table F2b published: November 2005
revised and updated: June 2008

3c	Gastroscopy with brush cytology	The cytology brush is sheathed and therefore there is low risk of the working channel becoming contaminated with lymphoid tissue. Cytology is of negligible risk provided a sheathed technique is used.	No contact of lymphoid tissue with the working channel.	–	
3d	Gastroscopy and balloon dilatation of stricture (oesophagus or pylorus).	Balloon dilatation may disrupt submucosal lymphoid tissue, which could be transferred to the working channel as the balloon is retracted back into this channel.	Contamination would be through 'contact' and would be lower than biopsy. Modifying the technique to include removing the endoscope and used balloon as one (without retracting it back into the working channel) would minimise the risk.	–	This technique should be considered non-invasive ONLY if the endoscope and balloon are withdrawn from the patient as one (*i.e.* without retracting the balloon into the working channel) and the balloon is cut-off and destroyed.
3e	Gastroscopy and bougie dilatation of oesophagus.	Bougie dilatation over a guide wire involves disruption of submucosal tissue only when the endoscope has been withdrawn.	No contamination of the working channel with lymphoid tissue.	–	

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3f	Gastroscopy and polypectomy	Polypectomy snares use diathermy, which coagulates tissue and this adheres to the snare. Although the snare is sheathed it is possible for lymphoid tissue to contaminate the working channel.	Polyp tissue fragments are readily sucked into the working channel during and after polypectomy.	**+** (but see exception, right)	Some endoscopists advocate the use of slow continuous irrigation of the working channel with water during polypectomy in order to minimise the risk of polyp fragments coming into contact with the internal surface of the endoscope working channel. Experience is, however, limited, and if polyp fragments become aspirated into the working channel (as is normally the case) the procedure is immediately deemed invasive.
3g	Gastroscopy and endoscopic mucosal resection (EMR)	The risks are the same as for polypectomy but the disruption of submucosal lymphoid tissue will be greater. A diathermy current is used and tissue will adhere to the snare.	Polyp tissue fragments are readily sucked into the working channel during and after EMR.	**+** (but see exception, right)	Some endoscopists advocate the use of slow continuous irrigation of the working channel with water during polypectomy in order to minimise the risk of polyp fragments coming into contact with the internal surface of the endoscope working channel. Experience is, however, limited, and if polyp fragments become aspirated into the working channel (as is normally the case) the procedure is immediately deemed

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					invasive.
3h	Gastroscopy or enteroscopy and argon plasma coagulation	In theory the technique involves no contact with the mucosa. However contact frequently occurs and tissue adheres to the catheter.	Tissue is likely to enter the working channel.	+	
3i	Gastroscopy and use of heater probe	Can be used to arrest bleeding but tissue may adhere to the probe and contaminate the working channel.	Lymphoid tissue contamination of the working channel is possible.	+	Heater probe should be discarded after use and disposed of by incineration.
3j	Gastroscopy and injection of ulcer	This may be a necessary procedure and haemostasis may be achieved through a variety of methods. Injection of adrenaline would not disrupt submucosal lymphoid tissue but there is contact between the needle and submucosal tissue.	Good technique would minimise risk. The needle is sheathed and therefore not in contact with the working channel. Poor technique might result in the unsheathed needle coming into contact with the channel, rendering the procedure invasive.	–	
3k	Gastroscopy and injection of varices	This may be a necessary procedure and haemostasis may be achieved through a variety of methods. Injection of a sclerosing agent would not disrupt submucosal lymphoid tissue but there is contact between the needle and submucosal tissue.	Good technique minimises the risk. The needle is sheathed and therefore not in contact with the working channel. Poor technique might result in the unsheathed needle coming into contact with the channel, rendering the procedure invasive.	–	

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3l	Gastroscopy and banding of varices	Bands are applied to prominent veins in the oesophagus. Submucosal lymphoid tissue should not be disrupted and in theory the risk should be low.	Tissue does not come into contact with the working channel during banding.	–	
3m	Gastroscopy and mucosal clipping	No disruption of lymphoid tissue.	No contamination of biopsy channel with lymphoid tissue.	–	
3n	Gastroscopy and insertion of a PEG (Percutaneous Endoscopic Gastrostomy) feeding tube	Patients with vCJD may require a PEG feeding tube. Contamination of the biopsy channel is possible with some techniques.	The most common 'pull through' method does involve a needle penetrating the stomach via the abdominal wall. In theory a small amount of submucosal lymphoid tissue might adhere to the needle and transfer to the wire or thread, which is pulled up via the working channel. However, the wire or thread can be withdrawn without entering this channel if the technique is modified so that the endoscope and wire or thread are withdrawn with the grasping device in full view (*i.e.* not withdrawing the wire or thread into the endoscope).	– if modified technique is used	Non-endoscopic (radiological) gastrostomy is recommended if possible. However, if this is not an option, the modified PEG technique must be used. This means that the endoscope and wire or thread are withdrawn with the grasping device in full view (*i.e.* the wire or thread is NOT withdrawn into the endoscope). If the wire or thread is withdrawn into the endoscope, the procedure must be considered invasive.
3o	Gastroscopy and stenting	No contact between working channel and lymphoid tissue.	Insertion of oesophageal stents does not disrupt lymphoid tissue during placement as the endoscope has been withdrawn and even with rescoping the working channel is unlikely to become contaminated.	–	

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3p	Gastroscopy and drainage of pancreatic pseudocysts	This is an invasive procedure that is potentially liable to contaminate the biopsy channel.	Contact between working channel with gastric submucosal lymphoid tissue is possible.	+	
4	**ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATO-GRAPHY (ERCP)**				
4a	ERCP without sphincterotomy	It is unlikely that the endoscope will become contaminated.	No contamination of the working channel with lymphoid tissue.	–	
4b	ERCP with sphincteroplasty	There is a significant risk that the biopsy channel will become contaminated with lymphoid tissue.	It is necessary to withdraw the dilatation balloon via the working channel of the endoscope so contamination with lymphoid tissue is possible. Subsequent manoeuvres to remove stones from the bile duct using retrieval balloons or baskets could contaminate the duodenoscope working channel.	+	
4c	ERCP with sphincterotomy	The diathermy papillotomy knife used in this procedure frequently has adherent tissue and it is likely that the working channel could become contaminated with lymphoid tissue.	Adherent tissue may be deposited in the working channel as the sphincterotome is withdrawn. Subsequent manoeuvres to remove stones from the bile duct using retrieval balloons or baskets could also contaminate the duodenoscope working channel.	+	
5	**ENTEROSCOPY**				
5a	Enteroscopy without biopsy	Tissue contamination of the working channel is very unlikely.	No contamination would result from a straightforward diagnostic enteroscopy.	–	

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5b	Enteroscopy with biopsies	It is likely that the working channel will become contaminated with lymphoid tissue.	Contaminated tissue may be deposited in the working channel.	**+**	It may be feasible to perform biopsy non-invasively if long-sheathed biopsy forceps become available
6	**COLONOSCOPY**				
6a	Colonoscopy without biopsy	A diagnostic colonoscopy is unlikely to contaminate the working channel with submucosal lymphoid tissue.	No contamination would result from a straightforward diagnostic colonoscopy.	**–**	
6b	Colonoscopy and biopsy	It is likely that the working channel will become contaminated with ileal submucosal tissue or colonic submucosal lymphoid aggregates.	Contamination of the working channel very likely.	**+** (but see exception, right)	Sheathed biopsy, where feasible, may allow tissue sampling while avoiding the risk of working channel contamination. Following biopsy, the tip of the biopsy forceps is fully retracted into the sheath, the tip of which is kept protruding from the endoscope tip throughout. The practice of taking a single biopsy and removing the endoscope with the forceps protruding, and then severing it with wire cutters, is to be discouraged.

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6c	Colonoscopy and balloon dilatation procedure	Balloon dilatation of an inflammatory stricture would disrupt lymphoid tissue and contaminate the balloon.	Withdrawing the balloon through the working channel would contaminate the colonoscope.	**–**	This technique should be considered non-invasive ONLY if the endoscope and balloon are withdrawn from the patient as one (*i.e*. without retracting the balloon into the working channel) and the balloon is cut-off and destroyed.
6d	Colonoscopy and polypectomy	Coagulation of tissue which then adheres to the snare. Sometimes small polyps retrieved using the suction channel and a biopsy "trap" This would increase the risk of contamination with lymphoid tissue.	Polyp tissue fragments are readily sucked into the working channel during and after polypectomy.	**+** (but see exception, right)	Some endoscopists advocate the use of slow continuous irrigation of the working channel with water during polypectomy in order to minimise the risk of polyp fragments coming into contact with the internal surface of the endoscope working channel. Experience is, however, limited, and if polyp fragments become aspirated into the working channel (as is normally the case) the procedure is immediately deemed invasive.

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6e	Colonoscopy and endoscopic mucosal resection	As with biopsy, lymphoid tissue may contaminate the biopsy channel.	Tissue adheres to the snare which would have to be withdrawn through the colonoscope on most occasions. Polyp tissue fragments are readily sucked into the working channel during and after EMR.	**+** (but see exception, right)	Some endoscopists advocate the use of slow continuous irrigation of the working channel with water during EMR in order to minimise the risk of polyp fragments coming into contact with the internal surface of the endoscope working channel. Experience is, however, limited, and if polyp fragments become aspirated into the working channel (as is normally the case) the procedure is immediately deemed invasive.
6f	Colonoscopy and argon plasma coagulation	Adherent tissue is likely to contaminate the suction/biopsy channel.	Contact with lymphoid tissue frequently occurs and tissue adheres to the catheter. Tissue is likely to enter the working channel.	**+**	
6g	Colonoscopy and stenting	No contact between working channel and lymphoid tissue.	Insertion of colonic stents does not disrupt lymphoid tissue during placement as the endoscope has been withdrawn and even with rescoping the working channel is unlikely to become contaminated.	**–**	

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7	FLEXIBLE SIGMOIDOSCOPY				
7a	Flexible sigmoidoscopy	This diagnostic procedure is unlikely to result in contamination of the working channel.	No contamination of the channel with lymphoid tissue would occur.	–	For 'invasive' procedures the risks are identical to those procedures associated with colonoscopy (see above)

Notes

* Where intubation is via the nasal cavity the advice of the endoscopist performing the procedure should be sought to determine whether a risk of contamination of the endoscope with olfactory epithelium can be excluded with confidence. If such contamination cannot be excluded it is advised to intubate *via* an oral route or take precautions appropriate for medium infectivity tissues.

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Annex H

After Death

H.1 On the death of a patient defined in Table 4a in Part 4 of this guidance, the removal of the deceased 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 is placed in a body bag, which should be labelled as High-Risk or Danger of Infection prior to transportation to the mortuary, in line with normal procedures for deceased patients where there is a known infection risk. An infection control notification sheet should be completed and given to the undertakers concerned with the deceased. (A specimen sheet, similar to that included in the Health Services Advisory Committee guidance on “Safe working and prevention of infection in the mortuary and post-mortem room” (second edition, 2202) (HMSO. ISBN 07176 2293 2) is included at the end of this Annex).

Post-mortem examination

H.2 Post-mortem examinations are required in order to confirm a clinical diagnosis and the cause of death in patients with suspected CJD, vCJD or any other form of human prion disease. However, such procedures have the potential to expose pathologists and anatomical pathology technologists (APTs) to tissues containing high levels of infectivity. 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" (second edition, 2002). Specific information on neuropathological post-mortems in CJD cases has been published (1).

H.3 Only fully trained, competent staff should undertake any necessary post-mortem examination on patients defined in Table 4a. At least two people should be present during the examination: the pathologist assisted by one senior APT, with another APT (if required) to aid in the labelling of containers for tissue samples. Observers should be prohibited from entering the post-mortem room and should only observe via video or from a separate viewing gallery. APTs and others attending out of necessity should be fully trained, competent, understand all of the procedures for such post- mortem examinations, and made aware of the relevant history of the patient.

H.4 Post-mortem examinations on CJD cases can be undertaken in any mortuary subject to local risk assessment; however, if available, a “high-risk” post-mortem suite should be used. If a general post-mortem suite is used, the CJD post-mortem should not be performed while other post-mortems are in progress. Additionally, appropriate care should be taken to minimise contamination of the working environment.

H.5 In order to minimise contamination of the working environment, the examination may be carried out with the deceased in an open body bag with absorbent wadding alongside the body, to retain the body fluids. Examination of the brain is essential in a case of suspected CJD or vCJD, and absorbent wadding can be placed underneath

the head to contain the spread of blood when the scalp is reflected and CSF when the skull is opened. If preferred, the entire head can be enclosed within a large plastic bag during use of a bone saw to open the cranium. A hand saw or electric saw can be used, but if an electric saw is used then it should be a dedicated saw and only used for known or suspected CJD/vCJD. There should be no vacuum unit attached to the saw. The use of a bag to enclose the head during the opening of the skull and/or removal of the brain is an optional technique, but requires experience for optimal results. If a polythene bag is used, it should be fitted over the head and neck of the deceased, and a saw introduced through a hole in the bag, which may then be sealed with tape as necessary. The polythene bag (if used) and any soiled wadding should be incinerated after the post-mortem.

H.6 Any mortuary undertaking a CJD autopsy should be prepared to perform a full autopsy and to freeze samples of brain and other tissues for biochemical evaluation for PrP^{Sc}. If local facilities cannot or are not prepared to do this, or do not have the expertise or equipment to sample and store the frozen tissues, then the deceased should be moved to a regional centre where the required experience and facilities exist. Advice on autopsy protocols and arrangements for refund of any removal costs for CJD post-mortems are made through the National CJD Surveillance Unit – see below for further details:

National CJD Surveillance Unit,
University of Edinburgh
Western General Hospital
Edinburgh
EH4 2XU
UK

Tel: 0131 537 1980

Personal Protective Equipment

H.7 Disposable protective clothing should be worn during the post-mortem, including a theatre suit, gown or preferably a full disposable coverall, apron, hat, double gloves, and a full face visor or splash guard mask with visor which completely encloses the operator's head to protect the eyes and mouth. A full hood with battery-powered ventilation may also be suitable. Consideration should be given to the use of hand protection, such as armoured or cut-resistant gloves. Care should be taken when reconstructing in respect of needle stick injuries. The APT must not be rushed and be given sufficient time to perform this task safely.

H.8 Disposable mortuary instruments should be used wherever possible, and be incinerated after use. If it is not feasible to use all disposable instruments due to some not being available in a disposable format then, a set of dedicated instruments for use in *ALL definite, probable, possible* or *at risk* cases is recommended. Manual or electric saws may be used. Although the former do not create aerosols and are easier to decontaminate after use, they may present a greater risk of injury. If an electric saw is used, it is advisable to have a dedicated saw for the same reasons as

above. Instruments and mortuary working surfaces should be decontaminated following the guidance in Annex C. The deceased should be washed in accordance with local protocols.

H.9 In some instances, the relatives of the deceased may request that the body is dressed in clothes prior to viewing at the mortuary or at the funeral directors. This is best achieved at the end of the post-mortem, when the body can be dried and dressed and then placed in a clean body bag prior to viewing.

Anatomy and pathology teaching

H.10 Anatomy departments are advised not to accept for teaching or research purposes, bodies, body parts or organs from any patients defined in Table 4a. Departments should produce local policies to identify who is responsible for checking whether a potential donor may be in one of the defined categories. The extent of the checks necessary will vary with circumstances, but would normally include checking with those responsible for the donation and the medical staff involved in the care of the donor.

Undertakers and embalmers

H.11 The undertakers should receive an infection control notification sheet (see specimen form at the end of this Annex), appropriately completed, before handling the deceased. 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. Dressing and cosmetic work on deceased patients from this risk group may be undertaken if the usual precautions routinely used when dealing with the dead are observed.

H.12 When the diagnosis of CJD or vCJD is known or suspected it is advisable to avoid embalming procedures. When embalming is required by the family, because of the need to preserve the deceased's appearance for some time, or if the deceased is to be transported outside the UK, then it should be carried out in a facility that is fit for purpose and where the staff are trained, competent and qualified to do so. Single use needles should be used in embalming procedures. All embalmers should perform risk assessments of their premises to establish if they can facilitate embalming onsite, or if their company would need to refer any such request to a specialist establishment.

H.13 The embalming process involves replacing the deceased's blood with a fixative that often includes a dye in order to counter the paleness of the deceased's appearance. The process involves inserting a cannula into an artery (similar to a central line), usually the common carotid, and slowly perfusing the tissues with this fixative. An instrument known as a trocar is used to remove gas and excess fluids from the thoracic and abdominal cavities, prior to injecting fluid into them. A hypodermic syringe is used to inject any tissues that have received insufficient fluid from the arterial injection. A deceased patient who has undergone a post-mortem examination will be subject to a different procedure, which generally involves reopening the body, via the PM incisions, and locating and using the arteries inside the deceased.

Funerals and cremations

Viewing the deceased

H.14 Relatives, friends or carers of the deceased may wish to view or have some final contact with the deceased. Such viewing and possible superficial contact, such as touching or kissing, need not be discouraged even if a post-mortem has taken place. Body bags may be rolled down temporarily to allow superficial contact; there is no need to deny the relatives, friends or carers this opportunity if a post-mortem examination has been performed.

Return of tissues, blocks, slides etc.

H.15 If consent has been obtained for the retention of tissue for teaching, research and other scheduled purposes, none of the tissues retained following the post mortem examination are required to be disposed of. If this is not the case, following a request from relatives, friends, carers or a person in a Qualifying Relationship (2) decisions about whether tissues, blocks, slides etc of a patient defined in Table 4a can be returned, should be made on the basis of an assessment of the risks. Respectful disposal of tissue by the hospital may be preferable. Each establishment will have their chosen method of respectful disposal, which should be in keeping with the Human Tissue Authority's Code of Practice. If a risk assessment indicates that these items may be returned, this is best done *via* the funeral director. If return is not possible, families should have the reasons explained to them. Any retained items from such situations should only be returned, with information relating to the potential risks from the material (*e.g.* infection or chemical exposure), so that relatives can consider all the risks before selecting the most appropriate option for immediate respectful disposal. Care must be taken to ensure confidentiality in all dealings between funeral directors and a patient's relatives.

Environmental concerns

H.16 There is no need to discourage burial of a patient with known or suspected CJD or vCJD, and no special arrangements for burial are required. Similarly, there is no need for any extra precautions to be taken for cremation.

Transporting the deceased

H.17 No additional precautions are 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. Any additional requirements of the individual carrier should be discussed on a case-by-case basis. The deceased will normally be required to have been embalmed prior to transport and a Notification of Infection form, to replace the usual free from infection form, must also be produced.

Exhumation

H.18 A Home Office licence is required before exhumation can take place. Those involved with such a procedure should follow normal standard practice for exhumations.

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The ACDP TSE Working Group are grateful to the Association for Anatomical Pathology Technology, the British Institute of Embalmers, Professor Sebastian Brandner, Imperial College London and Mrs Linda McCardle, National CJD Surveillance Unit, Edinburgh, for their valuable contribution to this guidance.

References

1. Ironside JW, Bell JE. The “high-risk” neuropathological autopsy in AIDS and Creutzfeldt-Jakob Disease: principles and practice. *Neuropathol Appl Neurobiol.* 1996; **22:**388-93.
2. Human Tissue Act 2004, Code of Practice on Consent, www.hta.gov.uk

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Specimen Infection Control Notification Sheet

Name of deceased: ……

Date and time of death: ……

Source hospital and ward: ……

The deceased's remains are a potential source of infection:

YES / UNKNOWN (see note 1 below) (ring as appropriate)

If **YES** (see note 2 below), the remains present an infectious hazard of transmission by: (ring as appropriate):

Inoculation **Aerosol** **Ingestion**

Instructions for handling remains (If **YES** above, tick as appropriate):

Body bagging	☐
Embalming presents high risk	☐

Signed: (Note 3) ……..

Print name ……..

On behalf of: ……..… (hospital / mortuary / General Practitioner)

Notes

Note 1: Not all infected patients display typical symptoms, therefore some infections may not have been identified at the time of death.

Note 2: In accordance with health and safety law and the information provided in the Health Services Advisory Committee guidance *Safe working and the prevention of infection in the mortuary and post-mortem room* (Second edition 2002).

Note 3:

- In hospital cases, the doctor certifying death, in consultation with ward nursing staff, is asked to sign this Notification sheet;
- Where a post-mortem examination has been undertaken, the pathologist is asked to sign this Notification Sheet;
- In non-hospital situations, the doctor certifying death is asked to sign this Notification Sheet.

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ANNEX I

Outline Protocol for Management of Instruments and Tissues from Brain Biopsy Procedures on Patients with Progressive Neurological Disorders

The Department of Health has taken expert advice on the need for additional guidance on the quarantine of surgical instruments following brain biopsies.

The Chief Medical Officer issued a protocol for management of surgical instruments and tissues from brain biopsy procedures on patients with progressive neurological disorders on 17 May 2004.

This protocol is attached as the next 4 pages of this document.

17th May 2004

Dear Colleague

REDUCING THE RISK OF EXPOSURE OF PATIENTS TO THE AGENT OF CJD THROUGH BRAIN BIOPSY PROCEDURES

A brain biopsy can reveal a diagnosis of CJD that was not suspected prior to the biopsy because CJD can present in atypical ways with a differential diagnosis that includes conditions such as cerebral vasculitis. The biopsy could result in inadvertent exposure of subsequent patients to CJD agent via the instruments used. The Department of Health has taken expert advice on the need for additional guidance for the quarantine of surgical instruments following brain biopsies in such circumstances.

The attached protocol has been prepared in conjunction with neurosurgeons, neurologists, neuropathologists and the National CJD Surveillance Unit.

I strongly urge that this protocol be implemented within your NHS Trust with immediate effect.

National guidance "Transmissible Spongiform Encephalopathy Agents: Safe Working and the Prevention of Infection"[1] on the prevention of infection arising from the agents that cause Creutzfeldt-Jakob Disease (CJD) and other spongiform encephalopathies was last revised and issued in December 2003.

I would be grateful if Medical Directors would also review present policies, procedures and practices within your NHS Trusts to ensure that this guidance is being fully complied with and that all staff in key roles are aware of it and fully understand how to apply it. The protocol for brain biopsy developed by the Department of Health has been added as an Annex to this Guidance.

Liz Donaldson

Sir Liam Donaldson
Chief Medical Officer

From the Chief Medical Officer

Sir Liam Donaldson
MSc,MD,FRCS(Ed),FRCP,FFPHM

Richmond House
79 Whitehall
London SW1A 2NS

PL/CMO/2004/2
Gateway Reference: 3105

For Action
- Medical Directors of NHS Trusts
- Neurologists
- Neurosurgeons
- Pathologists

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PO Box 777, London SE1 6XH

Email: doh@prolog.uk.com

For correction of any discrepancies in changes of address, practice or name, please contact:
The Medical Mailing Company
PO Box 60, Loughborough
Leicestershire LE11 0WP
Tel: Freephone 0800 626387

This letter is also available on the Internet at:
http://www.dh.gov.uk/cmo

[1] www.dh.gov.uk > Policy and Guidance>Health and Social Care Topics >CJD >CJD publications > Transmissible Spongiform Encephalopathy Agents: Safe Working and the Prevention of Infection.

Outline Protocol for Management of Instruments and Tissues from Brain Biopsy Procedures on Patients with Progressive Neurological Disorders

Department of Health 2004

CJD can present in atypical ways with a differential diagnosis that includes conditions such as cerebral vasculitis. A brain biopsy therefore could reveal a diagnosis of CJD that was not suspected prior to the biopsy. The protocol below minimises the risk that this could result in inadvertent exposure of subsequent patients to CJD agent via surgical instruments.
A single person involved in the clinical care of the patient should take responsibility for co-ordination of the procedures and communications, including alerting the neuropathology laboratory in advance of sending samples and monitoring all aspects of the protocol.

A. Clinical assessment and biopsy procedure

1. This protocol should apply to all patients who have unexplained progressive dementia (or ataxia or neuropsychiatric syndromes) in whom diagnostic brain biopsy is considered appropriate in order to establish or exclude a diagnosis.
2. The neuro-radiology in such patients usually shows no evidence of a space-occupying lesion.
3. The patient does not fulfil the WHO criteria[2] for probable or possible CJD [3]. Indeed CJD may not have been considered on clinical grounds.
4. Brain biopsy, preferably an open block biopsy, is performed for diagnosis.

B. Handling the neurosurgical instruments and the biopsy tissues

5. Single use instruments should be used wherever possible without compromising patient safety.
6. Any instruments that may have come into contact with brain or meninges of patients identified (A) should be washed at the point of use and quarantined immediately after use[4]
7. Send the tissue samples from the biopsy procedure unfixed directly to the neuropathology laboratory, ideally within 10 minutes of collection.
8. In the neuropathology laboratory, using containment conditions appropriate for fresh human brain, remove a small portion of unfixed cortical grey matter (at least 0.1g) from the biopsy. Store the sample frozen, clearly labelled, and preferably at -70^{o}C (-20^{o}C is sufficient for storage for several weeks) in a designated freezer.
9. Fix the remainder of the tissue samples in formalin and process into paraffin wax.

[2] The WHO criteria can be found at www.cjd.ed.ac.uk

[3] Precautions to be taken for procedures on symptomatic patients with possible or probable CJD, or when CJD is under active consideration are set out in the ACDP/SEAC TSE Joint Working Group Guidance, which can be found at www.dh.gov.uk > Policy and Guidance>Health and Social care Topics>CJD>CJD Publications>Transmissible spongiform encephalopathy agents: Safe working and the prevention of infection.

[4] Annex E of the above guidance for guidance on quarantine of instruments

C. Neuropathological diagnosis and the fate of the neurosurgical instruments

10. **If a definite diagnosis of a disorder other than CJD is made** (and there is no other evidence to suggest any form of CJD).
    - The neurosurgical instruments can be reprocessed and reused.

11. **If a definite diagnosis of CJD is made**
    - Destroy the neurosurgical instruments[5] and refer the case to NCJDSU by the clinician responsible for the patient (a request to review the biopsy will be made as part of NCJDSU's routine activities). Precautions to minimise the risk of transmission as a result of procedures carried out in the pathology laboratory and the clinic should be taken in accordance with the ACDP/SEAC TSE Guidance.

12. **If the diagnosis is uncertain**
    - If the local neuropathologist cannot exclude CJD as a possible diagnosis, contact NCJDSU to refer the case for further investigation. NCJDSU will arrange uplift and transport of the fixed and frozen tissues.
    - If an alternative diagnosis is made by the NCJDSU, the neurosurgical instruments can be reprocessed and reused.
    - The neurosurgical instruments should be destroyed[4], if a definite diagnosis of CJD is made by NCJDSU.
    - If the diagnosis remains uncertain, the neurosurgical instruments should remain in quarantine until a definite diagnosis is made, or the patient dies. Precautions to minimise the risk of transmission as a result of procedures in the pathology laboratory and the clinic should be taken in accordance with the ACDP/SEAC TSE Guidance[2] .

13. **If the patient dies without a diagnosis**
    - Seek consent for postmortem examination of the brain and, if it is given, follow the procedures set out in box 12 above.
    - The instruments used for the biopsy should be destroyed[4], if consent for postmortem examination is not given.

    - If the diagnosis is still uncertain after post-mortem examination of the brain, the instruments used for biopsy should be destroyed[4].

[5] Certain instruments can be used as a resource for research. Please contact the Department of Health (John.Stephenson@doh.gsi.gov.uk / 0207 972 5607) to arrange for collection of any surgical instruments that would otherwise be destroyed.

D Flow diagram of essential communications

A single person, usually the consultant neurologist responsible for the patient's care, should ensure that the relevant information is communicated to the appropriate people.

STEP	*INFORM*	*ACTION*
Brain biopsy planned on a patient identified in Box A	**IC Team /SSD**	**quarantine instruments**
	Neuropathology Lab	**process and store biopsy sample**
Neuropathologist excludes CJD as a diagnosis	**IC Team/SSD**	**release quarantined instruments**
Neuropathologist diagnoses CJD	**IC Team/SSD**	**destroy instruments[1]**
	NCJDSU	**CJD surveillance**
	National Prion Clinic	**Consideration for clinical trial**
Neuropathologist neither diagnoses nor excludes CJD	**NCJDSU**	**diagnosis**
NCJDSU gives non-CJD diagnosis	**IC Team/SSD**	**release quarantined instruments**
NCJDSU diagnoses CJD	**IC Team/SSD**	**destroy instruments[1]**
	CCDC	**report to CJDIP**
NCJDSU neither diagnoses or excludes CJD	**IC Team/SSD**	**continue quarantine of instruments**
	CCDC	**report to CJDIP**
Patient dies without diagnosis and post mortem is not permitted	**IC Team/SSD**	**destroy instruments[1]**
	CCDC	**report to CJDIP**

[1] Certain instruments can be used as a resource for research. Please contact the Department of Health (John.Stephenson@doh.gsi.gov.uk / 0207 972 5607) to arrange for collection of any surgical instruments that would otherwise be destroyed.

Abbreviations used

IC	Infection control
SSD	Sterile Services Department
NCJDSU	National CJD Surveillance Unit
CCDC	Consultant in Communicable Disease Control
CJDIP	CJD Incidents Panel

ANNEX J

Assessment to be carried out before surgery and/or endoscopy to identify patients with, or at increased risk of, CJD or vCJD

Summary of advice (revised January 2014)

Annex J provides a clear and pragmatic way of assessing CJD and vCJD risk prior to surgery or endoscopy. Certain groups of patients have been informed that they are at increased risk of CJD or vCJD. Therefore it is recommended that all patients about to undergo any surgery or endoscopy should be asked if they have ever been notified as at increased risk of CJD or vCJD. This recommendation is outlined in paragraphs J1 and J2.

In addition, patients undergoing surgery or neuro-endoscopy which may involve contact with tissues of potentially high level TSE infectivity ("high risk tissues") should, through a set of detailed questions, be assessed for their possible CJD/vCJD risk exposure. These questions are outlined in Table J1 and paragraphs J3 to J6.

Previous revision date: January 2013
Changes new to this edition:

Date	Change	Notes
January 2014	Alignment of the list of people considered at increased risk of vCJD with that contained in Part 4.	This change affects paragraph J14.
January 2014	Change of terminology from "infection control" to "infection prevention and control"	Changed throughout the document as appropriate

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Recommendation for all surgical and endoscopy patients

J1. The CJD Incidents Panel has identified a number of individuals or groups who are at increased risk of CJD or vCJD (see paragraphs J14 – J18).

At a local level arrangements should be put in place to ensure that patients who have been notified they are at increased risk of CJD/vCJD are identified before surgery or endoscopy, to allow appropriate infection prevention and control procedures to be followed.

All patients about to undergo **any** elective or emergency surgical or endoscopic procedure should be asked the question:

"Have you ever been notified that you are at increased risk of CJD or vCJD for public health purposes?"

J2. The actions to take following the patient's response to the above question are:

Patient's response	Action
No	Surgery or endoscopy should proceed using normal infection prevention and control procedures unless the procedure is likely to lead to contact with high risk tissue.
Yes	Please ask the patient to explain further the reason they were notified. Special infection prevention and control precautions should be taken for all surgery or endoscopy involving contact with medium or high infectivity tissues (see Annex A1) and the local infection prevention and control team should be consulted for advice. Part 4 of this Guidance provides advice on the precautions to be taken during the treatment of patients with or at increased risk of CJD or vCJD, and Annex F provides information on endoscopic procedures. The patient's response should be recorded in their medical notes for future reference.
Unable to respond	Surgery or endoscopy should proceed using normal infection prevention and control procedures **unless** the procedure is likely to lead to contact with high risk tissue. If this is the case, please refer to the additional recommendations for high risk procedures from paragraph J3 onwards, with particular reference to paragraphs J7 – J10.

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Additional recommendations for surgery and neuro-endoscopy which may involve contact with high risk tissue only

N.B. These additional recommendations are only applicable to those assessing patients in neurosurgical and ophthalmic surgical departments for intradural and posterior ophthalmic surgical procedures. With regards to endoscopy, these additional recommendations are only applicable to those assessing patients for intradural neuro-endoscopic procedures.

Procedures should not be delayed whilst information is being collected, and clinicians should be careful not to prejudice overall patient care.

J3. As well as asking all patients whether they have been notified as being at increased risk of CJD/vCJD, clinicians assessing patients for procedures that involve contact with high risk tissues should ask supplementary questions (as outlined in Table J1) to assess further their CJD/vCJD risk. If a patient has answered 'yes' to the question in paragraph J1 there is no additional need to ask the questions in Table J1 – the patient's risk status has been established.

J4. Tissues assumed or proven to have high level infectivity for CJD or vCJD are:

- Brain
- Spinal cord
- Implanted dura mater grafts prior to 1992
- Cranial nerves, specifically:
    - the entire optic nerve
    - only the intracranial components of the other cranial nerves
- Cranial nerve ganglia
- Posterior eye, specifically:
    - posterior hyaloid face
    - retina
    - retinal pigment epithelium
    - choroid
    - subretinal fluid
    - optic nerve
- Pituitary gland

Annex A1 gives further advice on CJD/vCJD tissue infectivity

J5. Table J1 outlines recommended questions to assess CJD/vCJD risk. It is recommended that patients are asked these questions prior to elective or emergency surgical or neuro-endoscopic procedures likely to involve contact with tissues of potentially high infectivity. Paragraph J6 outlines the steps to take based on the patient's responses. Appendix B is an information sheet for pre-surgical patients undergoing surgery or neuro-endoscopy on high risk tissues about the questions they will be asked.

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Table J1 – CJD risk questions for patients about to undergo elective or emergency surgical or neuro-endoscopic procedures likely to involve contact with tissues of potentially high level infectivity

	Question to Patient	Notes to clinician
1	Have you a history of CJD or other prion disease in your family? If yes, please specify.	Patients should be considered to be at risk from genetic forms of CJD if they have or have had: i) Genetic testing, which has indicated that they are at significant risk of developing CJD or other prion disease; ii) A blood relative known to have a genetic mutation indicative of genetic CJD or other prion disease; iii) 2 or more blood relatives affected by CJD or other prion disease
2	Have you ever received growth hormone or gonadotrophin treatment? If yes, please specify: i) whether the hormone was derived from human pituitary glands ii) the year of treatment iii) whether the treatment was received in the UK or in another country	Recipients of hormone derived from human pituitary glands, e.g. growth hormone or gonadotrophin, have been identified as at increased risk of sporadic CJD. In the UK, the use of human-derived growth hormone was **discontinued in 1985** but human-derived products may have continued to be used in other countries. In the UK, the use of human-derived gonadotrophin was **discontinued in 1973** but may have continued in other countries after this time.
3	Have you ever had surgery on your brain or spinal cord?	(a) Individuals who underwent intradural brain or intradural spinal surgery before August 1992 who received (or might have received) a graft of human-derived dura mater are "at increased risk" of transmission of sporadic CJD (unless evidence can be provided that human-derived dura mater was not used). (b) NICE guidance emphasises the need for a separate pool of new neuroendoscopes and reusable surgical instruments for high risk procedures on children born since 1st January 1997 and **who have not previously undergone high risk procedures**. These instruments and neuroendoscopes should not be used for patients born before 1st January 1997 or those who underwent high risk procedures using reusable instruments before the implementation of this guidance.

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J6. **The actions to be taken following the patient's response to the above questions are:**

Patient's response	Action
No to **all** questions	Surgery or neuro-endoscopy can proceed using normal infection prevention and control procedures.
Yes to **any** of questions **1, 2 or 3**	Further investigation into the nature of the patient's CJD risk should be undertaken, and the patient's CJD risk assessed. This assessment of CJD risk should be recorded in the patient's medical notes for future reference. If the patient is found to be at increased risk of CJD or vCJD following investigation, or the risk status is unknown at the time of the procedure, special infection prevention and control precautions should be taken for the patient's procedure including quarantining of instruments, and the local infection prevention and control team should be consulted for advice. Part 4 of this guidance provides advice for the precautions to be taken during the treatment of patients with or at increased risk of CJD or vCJD, and Annex F provides information on neuro-endoscopic procedures. If the patient is found to be at increased risk of CJD or vCJD they should also be referred to their GP, who will need to inform them of their increased risk of CJD or vCJD and provide them with further information and advice. This is available from the CJD Incidents Panel: http://www.hpa.org.uk/CJDIncidentsPanel Patients who are at increased risk of genetic forms of CJD should be offered the opportunity of referral to the National Prion Clinic, based at the National Hospital for Neurology and Neurosurgery, Queen Square, London: http://www.nationalprionclinic.org/ Patients who are at increased risk of sporadic CJD due to receipt of human-derived growth hormone or gonadotrophin should be offered the opportunity of referral to the UCL Institute of Child Health, London. Contact: leahdavidson@msn.com, 020 7404 0536
Unable to respond	See paragraphs J7 – J10 below for advice.

Emergency surgery or neuro-endoscopy which may involve contact with high risk tissue

J7. In the event that a patient about to have emergency surgery or neuro-endoscopy is physically or otherwise unable to answer any questions, a family member, or someone close to the patient (in the case of a child, a person with parental responsibility), should be asked the CJD risk questions as set out in Table J1 prior to the surgery or neuro-endoscopy.

J8. If the family member, or someone close to the patient, is not able to provide a definitive answer to the CJD risk questions, the surgery or neuro-endoscopy should proceed but all instruments should be quarantined following the procedure (see Annex E of this guidance for details on quarantining). The patient's GP should be contacted after the surgery or neuro-endoscopy, and enquiries made as to whether the patient is at increased risk of CJD/vCJD according to the questions as set out in Table J1.

J9. The actions to be taken following the GP's response to the questions in Table J1 are:

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GP's response	Action
No to **all** questions	The instruments can be returned to routine use after undergoing normal decontamination processes.
Yes to **any** of questions **1, 2 or 3**	Further investigation into the nature of the patient's CJD risk should be undertaken, and the patient's CJD risk confirmed or rejected. Confirmation or rejection of CJD risk should be recorded in the patient's medical notes for future reference. If the patient is found to be at increased risk of CJD or vCJD following investigation then the quarantined instruments should be destroyed. Alternatively, instruments destined for disposal may instead be retained for research – refer to Annex E for details. The patient's GP should inform the patient that they are at increased risk of CJD or vCJD and provide them with further information and advice. This is available from: http://www.hpa.org.uk/CJDIncidentsPanel Patients who are at increased risk of genetic forms of CJD may benefit from discussions with the National Prion Clinic, based at the National Hospital for Neurology and Neurosurgery, Queen Square, London: http://www.nationalprionclinic.org/ Patients who are at increased risk of sporadic CJD due to receipt of human derived growth hormone or gonadotrophin may benefit from discussions with the UCL Institute of Child Health, London. Contact: leahdavidson@msn.com, 020 7404 0536
Uncertain about **any** of questions **1, 2 or 3**	The instruments should be kept in quarantine. The local infection prevention and control team should carry out a risk assessment, and they may wish to involve the local Control of Communicable Disease Consultant in this process. The outcome of the risk assessment should determine whether or not to return the instruments to routine use.

Additional actions to be taken during pre-surgery assessment for CJD risk

J10. In addition to asking the patient CJD/vCJD risk questions, the following actions should also be carried out before any surgical or endoscopic procedure involving contact with high risk tissue. The clinician undertaking the pre-surgery assessment should:

- Check the patient's medical notes and/ or referral letter for any mention of CJD or vCJD status
- Consider whether there is a risk that the patient may be showing the early signs of CJD or vCJD, i.e. consider whether the patient may have an undiagnosed neurological disease involving cognitive impairment or ataxia

J11. These actions, in conjunction with the CJD/vCJD risk questions, will minimise the chance of a CJD incident occurring and therefore reduce the risk of transmission of CJD or vCJD to subsequent patients.

Infection prevention and control guidance

J12. Part 4 of this Guidance provides advice on the special infection prevention and control precautions that should be taken for patients with, or at increased risk of, CJD or vCJD, and Annex F provides information on endoscopic procedures.

Patients at increased risk of CJD or vCJD

J13. As outlined in Table 4A in Part 4, a number of patients have been identified as at increased risk of CJD or vCJD on the recommendation of the CJD Incidents Panel. Paragraphs J15 to J17 provide some further information on these individuals and the steps taken to ensure that health care staff are informed of their risk status.

J14. Patients identified to be at increased risk include:

Related to blood transfusions

- People who have received blood or blood components from someone who went on to develop vCJD
- People who have given blood or blood components to someone who went on to develop vCJD
- People who have received blood or blood components from someone who has also given blood or blood components to a patient who went to develop vCJD
- People who have received blood or blood components from 300 or more donors since 1990 (additional information on how this group is defined can be found in the ACDP TSE guidance FAQ document[1]).

Related to surgery

- People who have had surgery using instruments that had been used on someone who developed CJD
- People who have had an intradural neurosurgical or intradural spinal procedure before August 1992
- People who have received an organ or tissue from a donor infected with CJD or at increased risk of CJD

Related to other medical care

- People who have been treated with certain UK sourced plasma products between 1990 and 2001
- People who have been treated with growth hormone sourced from humans (before 1985)
- People who have been treated with gonadotrophin sourced from humans (before 1973)
- People who have been told by a specialist that they have a risk of developing the genetic form of CJD

[1] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/209775/Frequently_Asked_Questions.pdf)

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J15. When someone is notified that they are at increased risk of CJD or vCJD, they are asked to take certain precautions to reduce the risk of spreading the infection to others. These include:

- Not donating blood, tissue or organs;
- Informing healthcare staff if they need to undergo an invasive surgical, medical or dental procedure;
- Informing a family member or someone close to them, in case they need emergency surgery or endoscopy in the future

J16. The individual's GP is asked to record the patient's CJD risk status in their primary care records. The GP should also include this information in any referral letter should the patient require invasive surgical, medical or dental procedures.

J17. Further information on the work of the CJD Incidents Panel is available on the HPA website: http://www.hpa.org.uk/CJDIncidentsPanel

Training

J18. Health services should ensure that healthcare staff conducting pre-surgery assessments receive instruction and/or training necessary to understand the reasons for asking these questions**. It is important that these questions are asked in a manner that does not cause undue anxiety, and therefore the questioner should be prepared and able to reassure the patient, and provide further information if needed. Information for patients is available from the CJD Incidents Panel website at: http://www.hpa.org.uk/CJDIncidentsPanel**

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Information for patients undergoing surgery or neuro-endoscopy on high risk tissues **Appendix B**

Part of your routine assessment before surgery includes some questions to find out whether you could have an increased risk of Creutzfeldt-Jakob disease (CJD). We will ask you:

Have you ever been notified that you are at risk of CJD or vCJD for public health purposes?

Have you any history of CJD or other prion disease in your family?

Have you ever received growth hormone or gonadotrophin treatment?

Have you had surgery on your brain or spinal cord at any time in the past?

What is CJD?

Creutzfeldt-Jakob disease (CJD) is a rare brain disorder that affects about 1 in a million people each year. CJD is thought to be caused by the build up in the brain of an abnormal form of a protein called a 'prion'. Unfortunately CJD is fatal, and as yet there is no known cure. There are different types of CJD, including variant CJD (vCJD). vCJD is caused by eating meat from cows infected with BSE.

How can CJD spread from person to person?

A person who is infected with CJD may have abnormal prion protein in their body for years before becoming ill. If that person has an operation, or donates blood, tissues or organs, during that time, the abnormal prion protein that causes CJD could spread to other patients.

Why are we asking you about CJD before your operation?

The abnormal prion protein that causes CJD is very hard to remove or destroy. If surgical instruments are used on a patient who is infected with CJD they may still have prion protein on them, even after they have been properly washed and disinfected. They could then spread CJD to other patients. This is particularly important for operations on the brain, spinal cord and the back of the eye as these parts of the body contain the largest amount of abnormal prion protein.

What have these questions got to do with CJD?

CJD has been spread in several ways and different groups of people may have an increased risk of CJD.

We ask whether there is anyone in your family who has had CJD because some types of CJD can be inherited. These types of CJD are caused by faulty genes and may be passed from parent to child.

We ask whether you have had surgery on the brain or spinal cord because some of these operations used to use grafts of 'dura mater' (the tough lining round the brain and spinal cord). Some of these grafts have been linked to CJD infection - these grafts are no longer used.

We ask whether you have been treated with growth hormone or gonadotrophin infertility treatment because these used to be prepared from pituitary glands. Some of these hormone treatments have been linked to CJD infection - these hormones are no longer used.

We ask whether you have had a large number of blood transfusions as this could be related to an increased risk of variant CJD (vCJD). vCJD is the type of CJD which is caused by eating meat from cows infected with BSE. vCJD can be spread through blood transfusions.

What happens if I answer 'Yes' to any of these questions?

If you answer 'Yes' to any of these questions, medical staff will now examine your medical records in more detail to determine whether or not you may have an increased risk of CJD.

What will happen then?

If you do have an increased risk of CJD special precautions will be taken with the surgical instruments used in your operation. Your GP will be informed and will ask you to come and discuss what this means in more detail.

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Please remember that the overall risk of CJD spreading by these routes is generally **very low.** These questions are an extra measure to prevent CJD spreading through surgery. **This should not affect the medical care you receive now or in the future.**

What if I don't have a GP?

The health protection unit for your area will make sure that another doctor discusses this with you.

Can I have a blood test to see if I am infected with CJD?

Unfortunately there is no blood test available yet which could show if you have CJD.

Where can I find out more?

The following organisations offer further information and support.

- Public Health England: www.hpa.org.uk/cjd
- CJD Support Network website: www.cjdsupport.net
- National CJD Surveillance Unit website: www.cjd.ed.ac.uk
- National Prion Clinic website: www.nationalprionclinic.org/

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Annex K

Guidelines for pathologists and pathology laboratories for the handling of tissues from patients with, or at risk of, CJD or vCJD

Introduction

K1. This guidance is aimed at pathologists and individuals working in pathology laboratories who handle tissues from patients. It aims to ensure that laboratory staff are aware of risk factors for Creutzfeldt-Jakob disease (CJD) or variant CJD (vCJD) prior to carrying out procedures on tissues.

For the purposes of this guidance document, sporadic CJD, iatrogenic (accidentally transmitted) TSE and genetic TSE will all be referred to under the umbrella name of 'CJD'. Variant CJD will be referred to as 'vCJD'.

K2. The following information is outlined in this Annex:

- How to identify a potential case of CJD or vCJD prior to handling tissues from a living patient, or performing an autopsy on a patient with a history of dementia or a progressive neurodegenerative disorder
- the procedures for handling tissues of high or medium levels of infectivity from patients with, or at risk from, CJD or vCJD
- what to do in the event that a routinely handled tissue sample is subsequently found to be from a patient with, or at risk of, CJD or vCJD

K3. Other relevant information already covered by the ACDP TSE Working Group guidance includes:

- general laboratory containment and control measures. These are covered by Part 3 of this guidance
- the handling of brain biopsy tissues from patients with progressive neurological disorders. This is covered by Annex I of this guidance
- the procedures needed for an autopsy on a patient with, or at risk of, all forms of CJD. This is covered by Annex H of this guidance

K4. An algorithm is included to enable easy decision making on the treatment of tissue samples from patients with or at risk of CJD or vCJD, based on patient diagnosis and tissue infectivity risk. If the tissue sample is not designated

high or medium risk as outlined in Tables K1 and K2, no special precautions are needed, and normal protocols may be followed.

Patient Classification

K5. Patients are classified as follows:

A) Symptomatic

Symptomatic patients are classified according to verified WHO clinical and pathological criteria for:

a. Sporadic CJD
b. Iatrogenic (accidentally transmitted) TSE
c. Genetic TSE (familial CJD, GSS and FFI), and;
d. variant CJD (vCJD)

More information is available in Annex B of this guidance.

B) Asymptomatic patients at risk of familial forms of CJD

A patient should be considered to be at risk from familial forms of CJD linked to genetic mutations if they have or have had:

a. Genetic testing, which has indicated that they are at significant risk of developing CJD or other prion disease
b. A blood relative known to have a genetic mutation indicative of familial CJD
c. 2 or more blood relatives affected by CJD or other prion disease

C) Asymptomatic patients at risk of CJD or vCJD from iatrogenic exposure

Risk	Patient at risk of CJD	Patient at risk of vCJD
Received hormone derived from human pituitary glands, e.g. growth hormone or gonadotrophin. In the UK, the use of human-derived growth hormone was discontinued in 1985, and the use of human-derived gonadotrophin was discontinued in 1973, but human-derived products may have continued to be used in other countries	Yes	No
Undergone intradural neurosurgical procedures or operations on the spinal cord prior to August 1992	Yes	No
Received blood, tissues or organs from a donor who went on to develop CJD or vCJD, or was at risk of CJD or vCJD	Yes	Yes

Risk	Patient at risk of CJD	Patient at risk of vCJD
Received blood components or plasma derivatives from implicated batches of blood (**this includes most adult haemophiliacs in the UK**)	No	Yes
Donated blood to an individual who was later found to have vCJD	No	Yes

K6. **Autopsy on patients with dementias, ataxia and other undiagnosed neurological disorders**

In patients with a history of a neurodegenerative disorder, including dementia and ataxia, where the diagnosis is uncertain, the possibility of CJD should be considered before the autopsy is undertaken. Based on the clinical criteria listed above, CJD should be considered when there is a history of progressive dementia of less than 2 years duration when accompanied by myoclonus, visual problems, ataxia, pyramidal or extrapyramidal features, or akinetic mutism. The results of EEG studies should be examined to see if changes suggestive of CJD were present, and a positive assay for 14-3-3 protein in the CSF may also support the diagnosis of CJD.

The National CJD Surveillance Unit can provide advice on individual cases upon request – please call 0131 537 1980.

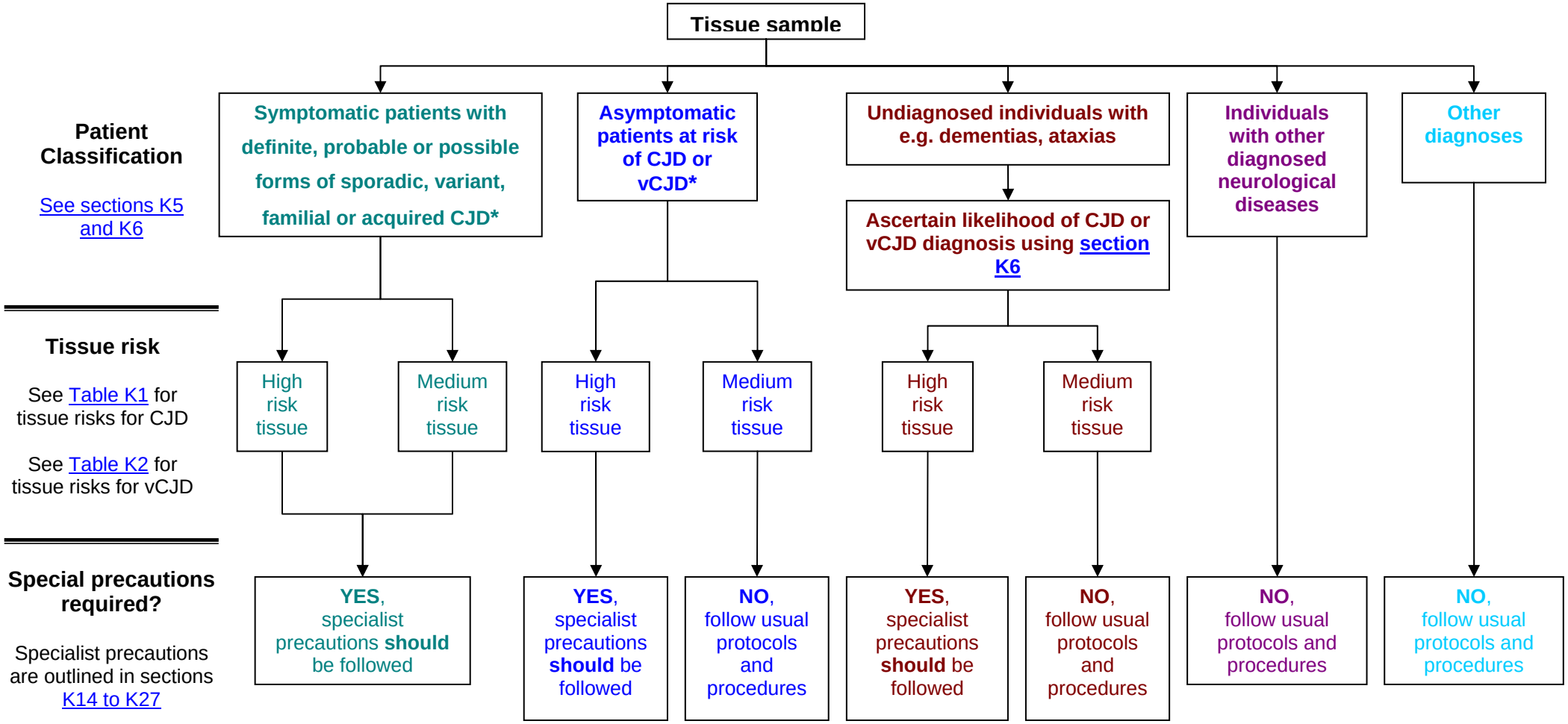
K7. **Autopsy on patients with known or suspected CJD or vCJD**

Annex H provides advice on autopsies on patients known or suspected to have CJD or vCJD.

Clinical information

K8. The clinical information on the request form accompanying the specimen should state the relevant information, and/or there may be such information on the hospital electronic patient record systems. If the patient is symptomatic, or asymptomatic but 'at risk', then the appropriate staff **must** be informed **prior** to any procedures being carried out. The samples should be handled only by fully trained staff who are aware of the relevant laboratory handling and health and safety guidelines.

Algorithm for the processing of tissue from patients with or at risk of CJD including vCJD



* See section K5

Table of tissues assumed to have medium or high level infectivity for CJD other than vCJD

K9. Table K1 outlines those tissues either assumed or proven to have medium or high level infectivity for CJD other than vCJD. This table is based on Table A1 in Annex A1 of this guidance, which is updated regularly in accordance with international guidelines. **Tissues assumed or proven to have either low level, or no, infectivity have not been included in this table, e.g. liver, kidney, muscle.**

Table K1 – tissues either assumed or proven to have medium or high level infectivity for CJD other than vCJD

Key: **+ve** = tested positive

-ve = tested negative

P = infectivity proven in experimental transmission studies

PrP^{TSE} = disease associated form of the prion protein

Tissue	Presence of abnormal prion protein and level of infectivity for CJD other than vCJD	
	PrP^{TSE} detected	**Assumed level of Infectivity**
Brain	+ve	High **P**
Spinal cord	+ve	High **P**
Dura mater*	-ve	High
Cranial nerves, specifically: o the entire optic nerve o only the intracranial components of the other cranial nerves	+ve	High
Cranial nerve ganglia	+ve	High
Posterior eye	+ve	High **P**
Pituitary gland	+ve	High
Spinal ganglia	+ve	Medium
Anterior eye and cornea**	-ve	Medium
Olfactory epithelium	+ve	Medium

* *Dura mater* is considered a high risk tissue, despite no PrP^{TSE} being detected. It is likely that *dura mater* used for grafting, and subsequently implicated in CJD transmission, could have been contaminated with brain tissue

** Anterior eye and cornea are considered medium risk, despite negative PrP^{TSE} tests, because corneal transplantation has been associated with CJD transmission

Notable omissions

K10. Peripheral tissues have been found to carry low levels of prion protein and/or infectivity in sporadic CJD. They are considered low risk due to a lack of epidemiological evidence of transmission risk.

K11. CSF and blood are classified as low risk tissues and do not require special precautions for biochemical or cytological investigations.

Table of tissues assumed to have medium or high level infectivity for vCJD only

K12. Table K2 outlines those tissues either assumed or proven to have medium or high level infectivity for vCJD. This table is based on Table A1 in Annex A1 of this guidance, which is updated regularly in accordance with international guidelines. **Tissues assumed or proven to have either low level, or no, infectivity have not been included in this table, e.g. liver, kidney, muscle.**

Table K2 – tissues either assumed or proven to have medium or high level infectivity for vCJD only

Key: **+ve** = tested positive

-ve = tested negative

NT = not tested

P = infectivity proven in experimental transmission studies

PrP^{TSE} = disease associated form of the prion protein

Tissue	**Presence of abnormal prion protein and level of infectivity for vCJD**	
	PrP^{TSE} detected	**Assumed level of infectivity**
Brain	+ve	High **P**
Spinal cord	+ve	High **P**
Dura mater*	-ve	High

Cranial nerves, specifically: o the entire optic nerve o only the intracranial components of the other cranial nerves	+ve	High
Cranial nerve ganglia	+ve	High **P**
Posterior eye	+ve	High
Pituitary gland	+ve	High
Spinal ganglia	+ve	Medium **P**
Anterior eye and cornea**	-ve	Medium
Olfactory epithelium***	NT	Medium
Tonsil	+ve	Medium **P**
Appendix	+ve	Medium
Spleen	+ve	Medium **P**
Thymus	+ve	Medium
Other lymphoid tissues (such as gut-associated lymphoid tissues and lymph nodes)	+ve	Medium **P**

* *Dura mater* is considered a high risk tissue, despite no PrP^{TSE} being detected. It is likely that *dura mater* used for grafting, and subsequently implicated in CJD transmission, could have been contaminated with brain tissue.

** Anterior eye and cornea are considered medium risk, despite negative PrP^{TSE} tests, because corneal transplantation has been associated with CJD transmission

*** Olfactory epithelium is considered medium risk, despite not having been tested for the presence of PrP^{TSE}, because PrP^{TSE} is present in the olfactory tract and bulb in CJD

Notable omissions

K13. Blood is considered to have a low risk of infectivity despite the four cases of vCJD infection that have been transmitted by contaminated blood transfusions. It is thought that the large volume and multiple infectious doses are important factors in transmission by packed red cells and other blood components. Blood is therefore classified as a low risk tissue and does not require special precautions for biochemical or cytological investigations

K14. CSF is classified as a low risk tissue and does not require special precautions for biochemical or cytological investigations.

Extra precautions for handling tissues with high or medium infectivity from patients with, or at risk of, all forms of CJD and vCJD

Trimming tissue

K15. Wearing the appropriate protective personnel equipment (PPE), **all fresh tissue** should be sliced or trimmed in a Class 1 Microbiological safety cabinet using cut resistant/steel mesh gloves and, when possible, disposable instruments. A disposable paper lining can be placed over the base of the cabinet to help contain splashes of contaminated formalin. After trimming, the cabinet should be wiped down with 2M sodium hydroxide and left for 1 hour. Do not use 20,000pmm sodium hypochlorite in cabinets as this will corrode the metal. Disposable instruments and sharps can be chemically decontaminated with 2M sodium hydroxide for 1 hour prior to placing them in a suitable container for disposal. Waste contaminated formalin should be absorbed into sawdust in a combustible stout container with lid prior to disposal. All this waste, including gowns, gloves and aprons should be sent for incineration. Non-disposable instruments and cut resistant/steel mesh gloves should be autoclaved or decontaminated with 2M sodium hydroxide for 1 hour.

K16. **Fixed tissues** can be trimmed either in a Class 1 Microbiological Safety cabinet or on a ventilated bench, taking care not to allow contamination of the surrounding laboratory space. Cleaning and disposal can be performed as above.

Treatment with formic acid prior to processing – to reduce infectivity

K17. Treatment with formalin appears to improve the action of the formic acid in reducing infectivity of the sample. The efficacy of formic acid in reducing infectivity in tissue samples from patients with CJD has been proven in the literature[1].

K18. Using a cabinet/fume cabinet, depending on local risk assessment, fixed tissue samples should be immersed in 96% formic acid for 1 hour. Samples must be thoroughly washed with water prior to further processing and examination.

[1] Brown P, Wolff A, Gajdusek DC. A simple and effective method for inactivating virus infectivity in formalin-fixed tissue samples from patients with Creutzfeldt-Jakob disease. Neurology. 1990; 40:887-90

K19. Formic acid is used normally in pathology laboratories to decalcify bones, and must be used in a cabinet/fume cupboard. It does not appear to harm the morphology of the tissues, so the results of subsequent tests are not jeopardised. In addition, plastic cassettes and other equipment are not affected. Tissues treated with formic acid can become slightly brittle, but this is not usually a major problem at the time of microtomy.

K20. **Following treatment with formic acid, tissues should be processed and handled like any other routine pathological specimen.** The processing fluids used on tissue blocks that have been exposed to formic acid (including high infectivity tissues e.g. brain) should not be treated as potentially contaminated and can be disposed of using routine precautions.

Microtomy

K21. Sections can be cut on a routine microtome using disposable blades. The blades should be discarded prior to cutting a different case. Disposable microtome blades are available, and are used routinely by many laboratories.

Frozen section work

K22. It is advised that **no** frozen section work should be done on **high risk tissues** for patients with, or at risk of, CJD or vCJD.

Disinfection and decontamination

K23. **Factors to consider when choosing chemical deactivation**

a. Sodium Hypochlorite

- Requires a dilution yielding 20,000 ppm available chlorine
- Must not be used on open surfaces i.e. benches due to harmful fumes
- Corrodes metal and steel - do not use on cabinets (max. only 5,000 ppm)
- Incompatible with formaldehyde, alcohols and acids – explosive
- Can be used for disinfecting glassware in a container within a cabinet
- Concentrated stock dilutions last for only approximately 2-3 weeks
- Diluted solutions are very unstable and should be made up daily

b. Sodium Hydroxide

- Use as 2M sodium hydroxide
- Should not be used on aluminium or zinc
- Will not cause fumes but corrosive to body tissue
- Irritant and harmful as dust

Table K3 – Decontamination and disposal

Item	Action	Contact Time
Formaldehyde-fixed tissues	Immersion in 96% formic acid (**unless** tissue has previously been exposed to phenol, which interacts deleteriously with formic acid)	60 minutes
Disposable clothing, paper tissues, etc	Double bag and dispose of by incineration	
Disposable sharps and instruments	Decontaminate with 2M sodium hydroxide for 1 hour. Collect in a suitable container, double bag and dispose of by incineration	
Non-disposable metal instruments	Soak in 2M sodium hydroxide, then autoclave at 134^{O}C with holding time of 3 minutes	60 minutes
Glassware including microscope slides	Collect in a suitable container, double bag and dispose of by incineration	60 minutes
Work surfaces / Microtome for non formic treated blocks	Flood with 2M sodium hydroxide, then wash well	60 minutes
Microbiological Safety Cabinets	Wash liberally with 2M sodium hydroxide, then wash well. Double bag filters and dispose of by incineration	60 minutes
Xylene, chloroform, contaminated water, contaminated fluids e.g. formalin, solvents *	Absorb on sawdust in a combustible stout container (with lid), double bag and then dispose of by incineration	
Paraffin wax and wax shavings	If tissues have been treated with formic acid, handle like any other routine pathological specimen. If not, collect in stout container (with lid) then dispose of by incineration	
CSF, Blood	Absorb on sawdust in a stout combustible container (with lid) then dispose of by incineration	60 minutes

* **For all liquid disposals, be careful to avoid dangerous chemical or explosive incompatibilities before disposal**

Decontamination of specialist equipment

K24. Providing other specialist pathology equipment is used after formic acid treatment, no decontamination of equipment is required.

Retrospective diagnosis of CJD following normal tissue sample processing

K25. The situation may arise whereby a patient is not suspected of having CJD, but is subsequently diagnosed following a biopsy or autopsy.

K26. The following needs to be taken into account when considering what action to take:

- The type of tissue involved
- The type of CJD that has been diagnosed
- How recently the diagnosis was made following the laboratory processes carried out on this tissue
- Whether the patient had clinical symptoms of CJD, or was in one of the "at risk" groups
- Whether the case has been notified to the National CJD Surveillance Unit (see section K28) and whether any of the tissue should be referred for further specialist investigations

K27. The following actions should be undertaken **(please note that these actions do not constitute best practice but reflect the best course of action to be taken under these particular circumstances)**:

a. Any samples taken from the patient should be traced, to ascertain what the tissue had been used for. Establish if any residual tissue was being stored
b. Fixed tissue should be double bagged and sent for incineration after the statutory 6 weeks. Prior to incineration, the NCJDSU should be contacted to ascertain whether they have a use for the tissue (see section K28)
c. Frozen tissue, including cryostat sections, should be fixed and then double bagged and sent for incineration after the statutory 6 weeks. Prior to incineration, the NCJDSU should be contacted to ascertain whether they have a use for the tissue (see section K28)
d. The paraffin blocks should be removed from main store and filed separately, clearly labelled as form of CJD and then stored separately. Reprocessing the blocks using formic acid is not required; the blocks can be sent for further investigations in the National CJD Surveillance Unit (see section K28)

e. Mounted (cover-slipped) slides can be filed as per usual

f. Un-mounted slides should be sent for incineration.

g. If it is still in use, the blade of the microtome used to cut the sample should be placed in a sharps box and this should be disposed of by incineration. The water in the water bath should be changed

h. **For brain banking**, identify the brass plates used for dissection of the CJD sample. They can no longer be used for the dissection or freezing of brain tissues. Prions are known to bind to metal surfaces, and washing with water will not guarantee the removal of prion infectivity. Frozen tissue from the next two cases received and cut fresh on the same brass plate following the CJD sample should be identified and withdrawn from research and either stored with appropriate biohazard labelling or transferred to the National CJD Surveillance Unit (see section K28).

   It is recommended that brass plates used on unfixed tissues in brain banks should be washed and soaked in sodium hypochlorite between dissections of new cases.

Where to send tissue samples for CJD testing

K28. If any tissue sample requires further investigations for the possibility of CJD infection, please contact Professor James Ironside or Mrs Linda McCardle in the National CJD Surveillance Unit on 0131 537 1980.

If any type of CJD has been diagnosed in an individual, please notify the National CJD Surveillance Unit on 0131 537 1980

ANNEX L

MANAGING CJD/vCJD RISK IN OPHTHALMOLOGY

Contents

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Introduction

L1. This guidance has been produced by the ACDP TSE Working Group Ophthalmology subgroup (membership list included as Appendix 5 of this document).

L2. Creutzfeldt-Jakob Disease (CJD) is an invariably fatal human disease belonging to the Transmissible Spongiform Encephalopathies (TSEs). These conditions are caused by a pathological accumulation in the brain of an aberrant form (PrP^{Sc}) of a normal cell surface glycoprotein, prion protein (PrP). CJD occurs in familial, sporadic and acquired (variant CJD and iatrogenic) forms. The familial forms of CJD are autosomal dominant traits associated with mutations in the prion protein gene (PRNP).

L3. At present, sporadic CJD (sCJD) is the most commonly encountered form of the disease with an incidence of 1 case per million, thus giving approximately 60 new cases per year in the UK. Patients with sCJD are predominantly in their 60s and as such come into contact with ophthalmologists through a range of unrelated ophthalmic conditions or because of visual symptoms caused by their condition.

L4. In the 1980s some British cattle developed bovine spongiform encephalopathy (BSE), probably from an altered form of the prion responsible for scrapie in sheep which had entered cattle feed. Human ingestion of BSE contaminated beef products is thought to have then led to the development of a new acquired form of the disease known as variant CJD (vCJD). The first case of vCJD was identified in the UK in 1994. Since then there have now been over 160 cases in the UK, typically in young adults.

L5. Although the majority of the human population of the UK was exposed at one time or another until 1996 to PrP^{Sc} by ingestion of contaminated beef products, the precise prevalence of preclinical infection of vCJD in the UK is unknown. The most reliable evidence we have to date is from the analysis of anonymised appendix and tonsil tissue taken from patients across the UK in 1995-1999. In this study, three positive samples were identified in the 12,674 samples tested, equating to a prevalence of approximately 1 in 4000 cases (237 per million). Although the infective risk of these preclinical cases is uncertain there is the obvious potential for iatrogenic transmission in a significant number of cases.

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L6. Iatrogenic CJD has been associated most recently with blood transfusion (3 clinical vCJD cases), and historically with human cadaveric growth hormone treatment (>190 cases), dura mater transplantation (>190 cases), contaminated neurosurgical instruments/EEG needles (6 cases) and corneal transplantation.

L7. There has been one definite case of CJD transmission from corneal transplantation reported, in the US in 1974. The patient, a 55-year-old woman, received a cornea from a donor with biopsy-proven sCJD. She developed a neurologic illness eighteen months after surgery and died 8 months later. The recipient's autopsy was positive for CJD. A further probable case of CJD transmission reported in Germany in 1997 was that of a 45-year-old woman who developed clinical symptoms and EEG evidence of sCJD 30 years after keratoplasty. The donor had biopsy-proven CJD but an autopsy of the recipient was refused. Several further possible cases of CJD transmission from corneal transplantation have been reported over the past 2 decades but it is uncertain as to the significance of the corneal transplantation in their subsequent CJD disease development. There are no other known cases of ophthalmic surgery or diagnostic procedure having resulted in CJD transmission between patients.

L8. Western blot analysis and immunohistochemistry of ocular tissues from sCJD and vCJD cases have found high levels of PrP^{Sc} in the retina, comparable to levels with cerebral cortex, and lower levels in the optic nerve. However, no detectable levels of PrP^{Sc} have been found in cornea, sclera, iris, lens, ciliary body vitreous or choroid. As prion proteins adhere strongly to materials including smooth metal surfaces and are not removed entirely by routine cleaning and autoclaving then there is the potential for iatrogenic transmission of PrP^{Sc} particularly during surgery involving the retina and optic nerve. Although the fact that PrP^{Sc} has not been found in other ocular tissues is reassuring, the demonstration of infectivity through transplantation suggests that practical precautions during diagnostic and surgical procedures are advisable to reduce the risk of iatrogenic transmission.

L9. Guidance has been issued previously by the Medical Devices Agency, the College of Optometrists, the Association of British Dispensing Opticians, the Royal College of Ophthalmologists and the National Institute for Health and Clinical Excellence (NICE) to reduce the risk of iatrogenic CJD transmission in ophthalmic care. The purpose of this latest document is to consolidate and update the available guidance and offer pragmatic solutions to aid implementation of such guidance.

Definition of anterior segment and posterior segment eye surgery or procedure

L10. Existing guidance has failed to clearly define anterior and posterior segment eye surgery or procedures for the purposes of CJD/vCJD risk. The ACDP TSE Working Group Ophthalmology Subgroup suggests the following definitions based on evidence of infectivity and presence of abnormal prion protein from animal and human studies:

a) **Posterior segment eye surgery or procedure** is defined as any surgery or procedure that involves potential contact with the posterior hyaloid face, retina, retinal pigment epithelium, choroid, subretinal fluid and optic nerve. Due to the high incidence of subretinal fluid drainage performed either intentionally or inadvertently during scleral buckling surgery, this form of surgery is considered as posterior segment surgery. See Appendix 1 for a list of posterior segment surgeries.

b) **Anterior segment surgery or procedure** is defined as any surgery or procedure involving ocular tissues other than those stated above, including:

- Ocular adnexal tissue including eyelids, periorbital tissue and lacrimal system
- Conjunctiva
- Cornea and limbus
- Iris
- Crystalline lens
- Anterior vitreous (excluding the posterior hyaloid face)
- Anterior vitrectomy performed via the cornea
- Extra-ocular muscle surgery
- Ciliary body
- Sclera (but not if allogeneic sclera used)
- Tissues of the orbit except optic nerve

See Appendix 2 for a list of anterior segment surgeries.

Definition of risk of surgical and diagnostic procedures

L11. The risk of iatrogenic transmission of CJD/vCJD during a surgical or diagnostic procedure is dependent on the risk of tissue infectivity and the nature of the procedure itself.

L12. **Any posterior segment eye surgery or procedure is considered high risk.**

L13. **Any anterior segment eye surgery or procedure is considered low risk.**

L14. The absence of any detectable abnormal prion protein in anterior segment tissue, the paucity of epidemiological evidence supporting iatrogenic transmission through anterior segment surgery and only a single definite case of iatrogenic transmission through corneal transplantation in 1974 (it is possible that the corneal tissue was contaminated by posterior segment tissue during processing) has led the ACDP TSE Working Group and its Ophthalmology Subgroup to propose anterior segment surgery or procedures as low risk for iatrogenic transmission.

L15. The stratification of surgery and diagnostic procedures into high and low risk of infectivity has various implications for the management of patients and instruments. These implications are detailed in this guidance.

Assessment of CJD/vCJD risk

L16. A local level policy should be put in place to ensure that all patients with or at increased risk of CJD/vCJD are identified before ophthalmic surgery to allow the appropriate infection controls to be followed.

L17. The ACDP TSE Working Group has issued advice for the assessment of patients' risk of CJD and vCJD before elective or emergency surgery and endoscopy in Annex J of their guidance. The following guidance for ophthalmic patients should be read in conjunction with Annex J.

L18. Any patient symptomatic of CJD/vCJD or considered at increased risk of CJD/vCJD should have their status recorded in their primary healthcare records. The GP should always include this information when referring patients for ophthalmic care. The clinical team undertaking pre-surgical assessment should check the patient's medical notes and/or referral information for any mention of CJD/vCJD status

Assessment for all elective and emergency ophthalmic surgery

L19. Annex J recommends that all patients about to undergo any elective or emergency surgery should be asked the question:

"Have you ever been notified that you are at increased risk of CJD or vCJD for public health purposes?"

The actions to be taken following the patient's response to the above question are outlined in paragraph J2 of Annex J.

Ophthalmic units should therefore ensure that all patients are asked this question prior to any elective or emergency ophthalmic surgery.

Additional assessment for posterior segment surgery

L20. Annex J also recommends that those patients about to undergo surgery which may involve contact with tissues of potentially high level TSE infectivity ("high risk tissues") should be assessed for CJD/vCJD risk through a set of detailed questions relating to possible exposure to CJD/vCJD outlined in Table J1 (see over). **For ophthalmic patients, only posterior segment eye surgery or procedures are defined as high risk**, as outlined in section L3 of this document and listed in Appendix 1. Ophthalmic units should therefore ensure that patients about to undergo a posterior segment eye procedure or surgery should be asked the CJD risk questions in Table J1 of Annex J (see over). Paragraph J6 of Annex J outlines the action to take based on the patient's responses.

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Annex J Table J1 – CJD risk questions for patients about to undergo elective or emergency surgical or neuro-endoscopic procedures likely to involve contact with tissues of potentially high level infectivity

	Question to Patient	Notes to clinician
1	Have you a history of CJD or other prion disease in your family? If yes, please specify.	Patients should be considered to be at increased risk from genetic forms of CJD if they have or have had: i) Genetic testing, which has indicated that they are at significant risk of developing CJD or other prion disease; ii) A blood relative known to have a genetic mutation indicative of genetic CJD or other prion disease; iii) 2 or more blood relatives affected by CJD or other prion disease
2	Have you ever received growth hormone or gonadotrophin treatment? If yes, please specify: i) whether the hormone was derived from human pituitary glands ii) the year of treatment iii) whether the treatment was received in the UK or in another country	Recipients of hormone derived from human pituitary glands, e.g. growth hormone or gonadotrophin, have been identified as at increased risk of sporadic CJD. In the UK, the use of human-derived growth hormone was **discontinued in 1985** but human-derived products may have continued to be used in other countries. In the UK, the use of human-derived gonadotrophin was **discontinued in 1973** but may have continued in other countries after this time.
3	Have you ever had surgery on your brain or spinal cord?	(a) Patients who underwent **intradural** neurosurgical or spinal procedures **before August 1992** may have received a graft of human-derived dura mater and should be treated as at increased risk, unless evidence can be provided that human-derived dura mater was not used. Patients who received a graft of human-derived dura mater **before 1992** are at increased risk of transmission of sporadic CJD, but **not** vCJD. (b) NICE guidance emphasises the need for a separate pool of new neuroendoscopes and reusable surgical instruments for high risk procedures on children born since 1st January 1997 and **who have not previously undergone high risk procedures**. These instruments and neuroendoscopes should not be used for patients born before 1st January 1997 or those who underwent high risk procedures using reusable instruments before the implementation of this guidance. [continued]

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4	Since 1980, have you had any transfusions of blood or blood components (red cells, plasma, cryoprecipitate or platelets*)? If yes, have you either: i) received more than 50 units of blood or blood components? **or** ii) received blood or blood components on more than 20 occasions? Where possible, please provide the names of all the hospitals where you received blood or blood components.	Patients who have received blood from more than 80 donors have been identified as at increased risk of vCJD. Information on this notification is available from the HPA: http://www.hpa.org.uk/vCJDpresurgicalassessment * This does not include: • Autologous transfusion • Plasma products such as IVIG, albumin, coagulation factors and anti-D

L21. Ophthalmic units with a mixed case load of anterior and posterior segment surgeries and procedures may wish to ask the questions in Table J1 of Annex J to all their patients for practical reasons. This is a local decision.

L22. As a separate pool of new posterior segment surgical instruments should be used for children born since 1 January 1997, and who have not previously undergone high risk procedures (see paragraph L38), it is important to correctly and reliably identify patients born since 1 January 1997 and ensure that they have had no previous high risk surgery which may have exposed them to risk of CJD/vCJD.

Emergency surgery

L23. Guidance on what to do if a patient about to undergo emergency surgery is physically or otherwise unable to answer any questions is included in paragraphs J7-J10 of Annex J.

Diagnostic examination, instruments and contact lenses

L24. There have been no known cases of iatrogenic transmission of CJD/vCJD resulting from diagnostic examination or contact lens wear. Although contact with the cornea is considered as low risk in terms of iatrogenic transmission of CJD/vCJD any steps that can further reduce potential risk of iatrogenic transmission are to be encouraged. A balance between pragmatism and a precautionary approach has been reached in the following advice.

L25. Instruments and contact lenses considered within this section include:

- Soft refractive and therapeutic contact lenses
- Rigid trial contact lenses, both corneal and scleral
- Tonometer prisms (Goldmann) and other contact tonometry devices
- Diagnostic contact lenses such as gonioscopes, fundus lenses, 3-mirror lenses
- Contact lenses used in therapy, often in conjunction with laser treatment, for example in capsulotomy, iridotomy, trabeculoplasty, retinopexy
- A- and B-scan ultrasound probes
- Electronic pachymeters
- Electrodes used in electrodiagnostic procedures such as electroretinography
- Prosthetic devices including trial or temporary artificial eyes

L26. The use of single-use instruments or contact lenses is recommended for use on those designated at increased risk of CJD or vCJD. Alternatively, the instruments or contact lenses should be quarantined and used solely on that individual patient. This latter approach could be problematic in ensuring mandatory sole use and thus the single-use instrument approach is considered more practical in these circumstances.

L27. The practice of single-use instruments or contact lenses for examination should be encouraged for other patients where cost and quality are acceptable. Several examples already exist in practice where potential iatrogenic transmission is reduced:

- Many services have adopted the use of disposable tonometry systems for intraocular pressure measurements in general settings and reserving reusable Goldmann tonometry for glaucoma clinics
- The use of non-contact biometry systems, for example IOLMaster
- The widespread use of soft trial contact lenses and therapeutic lenses

L28. This approach may not be practical for more specialised or complex instrumentation such as laser contact lenses and ultrasound probes.

L29. If reusable instruments or contact lenses are to be used it is imperative that they are cleaned and decontaminated in an acceptable and consistent way. Previous guidance regarding cleaning and decontamination of lenses and tonometry prisms involving 20,000ppm sodium hypochlorite is poorly adhered to, practised incorrectly (for example keeping tonometers wet after decontamination, varying concentrations of hypochlorite,

not changing the hypochlorite frequently enough) and carries the added risk of corneal burns.

L30. Generic guidance regarding cleaning, decontamination and storage of reusable instruments or contact lenses is outlined in Appendix 3. This generic advice includes disinfection steps to reduce significantly the problem of cross infection by conventional organisms such as viruses and bacteria, and thorough washing steps to reduce the level of residual protein and possible prion infectivity. The combination of measures is designed to reduce possible prion load and be practical in terms of risk reduction rather than risk elimination. Further guidance is available in the Royal College of Ophthalmologists publication "Ophthalmic Instrument Decontamination":
http://www.rcophth.ac.uk/docs/profstands/ophthalmic-services/DecontaminationApril2008.pdf

L31. It is accepted that the guidance in Appendix 3 may be difficult to adhere to in busy ophthalmic clinics. However it is important that it is followed, to reduce the risk of iatrogenic disease transmission. Pragmatic solutions to aid ophthalmic practitioners in this area include:

- Having a large subset of instruments (for example Goldmann tonometry prisms) which are used once each during a clinic, and following use are rinsed and kept wet. They can then be cleaned and decontaminated collectively at end of the clinic, according to the protocol in Appendix 3
- The possibility of using wholly disposable or non-contact systems for examination
- Encouraging procurement of non-contact or disposable covers for certain equipment, for example pachymeters or ultrasound probes
- Discussion with the local infection control team, decontamination team and/or microbiologist should be encouraged to promote best practice

L32. The practice of decontaminating tonometers with alcohol wipes alone is not sufficient to remove prion material, and may in fact fix the prion protein to the surface of the instrument.

Surgical management

Posterior segment eye surgery

Posterior segment eye surgery on patients with, or at increased risk of, CJD or vCJD

L33. Where possible, procedures should be performed with the minimum number of healthcare personnel required and at the end of the list, to allow normal cleaning of theatre surfaces before the next session.

L34. Single use instruments should be used if available provided they do not compromise the standard of clinical care. Following use, destroy all single-use items by incineration. This advice is also relevant to any instrument used during diagnostic procedures for such a patient.

L35. If reusable instruments are used they may be quarantined strictly for repeated use on the same patient. Facilities must be stringent for storage, identification and isolation of such instruments. Detailed guidance on the procedure for quarantining instruments, including initial washing to remove gross soil is available in Annex E of this guidance. If such instruments are to be reused on the same patient, they should be kept separate from other instruments whilst being cleaned and decontaminated e.g. in a separate basket in the washer disinfector. Alternatively the instruments must be disposed of by incineration.

L36. In cases of suspected CJD/vCJD the instruments can be quarantined as outlined above and returned to use after standard decontamination if a definitive alternative diagnosis is confirmed.

Posterior segment eye surgery on individuals not known to be infected and not at increased risk of CJD or vCJD

L37. The NICE interventional procedure guidance 196 “Patient safety and reduction of risk of transmission of Creutzfeldt–Jakob disease (CJD) via interventional procedures”, published in November 2006, states several important interventions that are specific to high risk posterior segment surgery. The guidance can be accessed here: http://www.nice.org.uk/nicemedia/pdf/ip/IPG196guidance.pdf. Specifically, it states that, for high risk surgical procedures (intradural operations on the brain and operations on the retina or optic nerve – ‘high risk tissues’):

- "Steps should be taken urgently to ensure that instruments that come into contact with high risk tissues do not move from one set to another. Practice should be audited and systems should be put in place to allow surgical instruments to be tracked, as required by Health Service Circular 2000/032: 'Decontamination of medical devices' and described in the NHS Decontamination Strategy"
- "Supplementary instruments that come into contact with high risk tissues should either be single-use or should remain with the set to which they have been introduced. Hospitals should ensure without delay that an adequate supply of instruments is available to meet both regular and unexpected needs"

L38. Pragmatic advice with regard to implementation of the NICE interventional procedure guidance 196 is outlined below:

a) Definition of the surgical set

i) The definition of a surgical set for posterior segment eye surgery is critical in implementing the NICE interventional procedure guidance 196. The greatest risk comes from instruments in contact with posterior segment tissues; however, splashes of vitreous or Hartmans's solution could theoretically carry infectivity to more distant locations

ii) **The surgical set is defined as any instrument that comes into contact with the eye during a procedure**

iii) Cryoprobes are considered part of the surgical set, but it may not be feasible to have a separate cryoprobe for each set. A pragmatic approach to this problem would be to ally a cryoprobe to specific sets to limit migration. For example, cryoprobe A would be used with sets 1, 2 and 3; cryoprobe B would be used with sets 4, 5 and 6, and so on. Alternatively, the use of indirect laser or the use of single-use endo-laser probes may be recommended

iv) Contact lenses used during surgery, irrigating or free standing, should also be defined as part of the set

v) Microscope or other non-contact indirect viewing systems, for example EIBOS or BIOM, are <u>not</u> considered part of the surgical set

b) Zero migration of instruments

i) Where reusable sets are used in high risk posterior segment surgery, zero migration of instruments must be adhered to and stringent tracking systems put in place

ii) It is estimated that the incidence of at least one instrument migrating into or out of a surgical set is as high as 50%. This high level of migration of instruments during high risk posterior segment surgery has the potential to promote a self-sustaining epidemic of CJD or vCJD

iii) Alternative pragmatic approaches to zero migration of instruments are outlined below:

- Provision of large surgical sets covering all surgical eventualities
- Provision of small surgical sets covering most surgical eventualities with the use of disposable instruments as supplements when required
- Provision of small surgical sets covering most surgical eventualities with the use of reusable instruments as supplements when required which stay with the new surgical set. Sufficient quantities of additional instruments will need to be purchased to allow for immediate availability of supplementary instruments if required or if instruments in sets are found to be defective or become unsterile during procedures
- Provision of small surgical sets covering most surgical eventualities with the use of clearly labelled reusable instruments as supplements, which are allied to a particular subset of surgical sets, and can be confidently tracked (e.g. cryoprobes)
- Exclusive use of single-use instrumentation. This is now possible for most, if not all, posterior segment surgical cases including external buckling surgery. When procuring single-use instruments it is imperative that the quality and performance of these instruments be equivalent to those of reusable instruments with appropriate procurement, quality control and audit mechanisms in place. Further advice is found in Appendix 4 of this document

c) Posterior segment surgery on children born since 1 January 1997

i) The NICE interventional procedure guidance 196 specifically advises the following on this issue:

"A separate pool of new neuroendoscopes and reusable surgical instruments for high risk procedures should be used for children born since 1 January 1997 (who are unlikely to have been exposed to BSE in the food chain or CJD through a blood transfusion) and who have not previously undergone high risk procedures. These instruments and neuroendoscopes should not be used for patients born before 1 January 1997 or those who underwent high risk procedures before the implementation of this guidance."

ii) It is therefore important to identify patients born since 1 January 1997 and make sure that they have had no previous high risk surgery which may have exposed them to risk of CJD

iii) A separate pool of new instruments should be used on this group of patients. However, it is important that this particular set does not become potentially infected through migration of other instruments into it, or its inadvertent use on patients born before 1 January 1997. This can be difficult to achieve confidently and thus it may be more practical in this group of patients to use single-use instruments. Where single-use alternatives are not practical, for example expensive instrumentation such as cryoprobes, mechanisms for the tracking, identification and storage of the new pool of reusable instruments should be stringent.

Anterior segment eye surgery

Low risk anterior segment eye surgery on individuals with, or at increased risk of, CJD or vCJD

L39. Although no special precautions such as quarantining or incinerating instruments is mandatory in these cases the general principles of reducing instrument migration and stringent tracking systems are encouraged.

L40. Due to the uncertainties of potential inadvertent contamination with tissues of high risk status during surgery then individual case by case assessment is required. In some circumstances, it may be appropriate to follow the precautionary guidance outlined for high risk posterior segment eye surgery (see paragraphs L33-37).

Low risk anterior segment eye surgery on individuals not known to be infected and not at increased risk of CJD or vCJD

L41. If any of the surgical procedures on low risk anterior segment eye tissues are complicated by surgery involving instruments coming into contact with the optic nerve or retinal tissue, the procedure should be considered as surgery on high risk posterior segment eye tissue.

L42. Although NICE guidance 196 specifically refers to ensuring zero migration of instruments in high risk posterior segment eye surgery it is considered desirable and good practice to limit migration of instruments between sets for low risk anterior segment eye surgery.

L43. Since Health Service Circular 2000/032: 'Decontamination of medical devices' all instrument trays must be identifiable and traceable. Tracking of all instruments or instrument trays is essential.

L44. Cleaning and decontamination of re-useable instruments should follow the decontamination advice outlined in paragraphs L54-55.

Ocular Tissue Transplantation

L45. The issue of ocular tissue transplantation is often confusing with regards to CJD risk assessment and actions required to reduce potential iatrogenic transmission. When assessing the risk, one must consider the nature of the surgical procedure (i.e. does the surgery involve high risk posterior segment surgery or low risk anterior segment surgery) and the potential infectivity of the donor material.

Transplant surgical procedure

L46. If the transplant surgical procedure involves high risk posterior segment surgery as defined in paragraph L10a then the precautions for high risk posterior segment surgery outlined in paragraphs L33-39 should be followed (e.g. potential future retinal pigment epithelium/retinal transplantation).

L47. If the transplant surgical procedure involves low risk anterior segment surgery as defined in paragraph L10b then the precautions for low risk anterior segment surgery outlined in paragraphs L40-45 should be followed (e.g. corneal transplantation).

L48. If allogeneic sclera is used as part of a surgical procedure (e.g. glaucoma tube surgery), the procedure is considered to be high risk posterior segment surgery because the

donor allogeneic sclera may have been in direct contact with the retina and optic nerve during processing. Thus the precautions for high risk posterior segment eye surgery should be used as outlined in paragraphs L33-39.

Potential infectivity of the donor material and recipient status

L49. On the currently available evidence, the risk of an ocular tissue donor in the UK having CJD/vCJD lies between 1.3 and 6.0 per 45 000. This risk is far less than the 1% threshold level of risk used by the CJD Incidents Panel to determine whether an individual would be considered as at increased risk of CJD/vCJD. Therefore, transplant recipients of:

- cornea
- limbal tissue
- sclera
- amniotic membrane
- ocular stem cells

should **not** be designated as at increased risk of CJD/vCJD due to iatrogenic exposure. The same will apply to recipients of retina and retinal pigment epithelium allograft if and when such procedures become available.

However, it must be noted that a recipient of any tissue or organ, including the above ocular tissues or cells, may not become a blood, tissue or organ donor. Organ donation from such individuals is not completely ruled out, but is considered on a case-by-case basis.

Records management

L50. Completion and return of the corneal, limbal and scleral transplant record and follow-up forms to NHSBT in a timely manner is a professional duty of ophthalmic surgeons, as stipulated by The Professional Standards Committee of the Royal College of Ophthalmologists.

L51. NHSBT, specifically the National Transplant Database maintained by ODT (Organ Donation and Transplantation), holds ocular tissue transplant records including donor and recipient details, the transplant record form and the transplant follow-up forms, which include the incidence of serious adverse reactions. If an ocular tissue transplant is not recorded on the National Transplant Database, the transplanting surgeon and the surgeon's hospital are legally responsible for ensuring the traceability of the tissue and maintenance of the two-way audit trail between donor and recipient.

L52. It is a statutory requirement under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 for eye banks to maintain records for a minimum of 30 years.

L53. A serious adverse events and reactions reporting mechanism has been developed by the Ocular Tissue Advisory Group (OTAG) and implemented by NHSBT for all ocular tissue transplants. This complements the statutory reporting mechanism for serious adverse reactions and events through the Human Tissue Authority. Forms are provided to the transplant surgeon with the tissue to be transplanted and should be retained in the patient's case notes. If at any stage a serious adverse reaction should occur (such as the development of CJD in the recipient) the reporting mechanism is commenced. The transplant follow-up forms also include a question regarding the occurrence of serious adverse reactions. Audit reports regarding issues of transplantation are reported to the Ocular Tissue Advisory Group.

Decontamination of surgical instruments

L54. Advice regarding decontamination of ophthalmic surgical instruments is available from the Royal College of Ophthalmologists publication "Ophthalmic Instrument Decontamination":
http://www.rcophth.ac.uk/docs/profstands/ophthalmic-services/DecontaminationApril2008.pdf
and from the forthcoming HTM01 01 series of documents (HTM01 01 A, B, C, D) which will cover, in detail, the decontamination of reusable medical and surgical devices.

L55. The following key points are considered in the above guidance:

a) Generic principles exist for the post-surgical handling/decontamination of ophthalmic instruments:
    i) their fine fragile nature which makes them prone to damage during cleaning processes
    ii) Fine bores which are difficult to clean
    iii) Instruments from single sets often require separation for cleaning and decontamination
b) Generic advice for cleaning and decontamination includes:
    i) Proper tracking systems for all ophthalmic instruments

ii) Maintain integrity of sets throughout the cleaning and decontamination process

iii) Keep instruments moist following surgery and prior to washing (this can be achieved either by use of sprays, mists or immersion – each of these have their own logistic issues)

iv) Thorough cleaning in washer-disinfectors

v) Promote use of specific washer-disinfector systems for ophthalmic instruments

vi) Work closely with the decontamination manager within the unit to identify issues and highlight training for staff involved in cleaning and decontamination

vii) Validation of systems within the unit and off-site Central Sterile Services Department (CSSD)

c) Good practice examples of cleaning and decontamination practices in UK and abroad should be highlighted

CJD incident management

L56. In relation to ophthalmology, a CJD incident occurs when there is a possibility that a patient or patients could have been exposed to CJD/vCJD through contaminated surgical instruments that were previously used on a patient with, or at increased risk of, CJD/vCJD. Such incidents occur 6-14 times per year (mean 9.7 times) in UK ophthalmic units.

L57. The CJD Incidents Panel advises on how to manage these incidents, and how to manage patients who could have been exposed to CJD/vCJD. Local infection control teams and health protection teams should seek advice from the CJD Incidents Panel on how to manage these incidents. Information sheets for clinicians and patients on CJD/vCJD can be found at: http://www.hpa.org.uk/CJD

L58. **All incidents should be reported to the CJD Incidents Panel secretariat**:
The CJD Incidents Panel Secretariat, Health Protection Agency – Centre for Infections, 61 Colindale Avenue, London NW9 5EQ
Tel: 020 8327 6411, Email: cjd@hpa.org.uk,

L59. The website http://www.hpa.org.uk/CJDIncidentsPanel includes the CJD Incidents Panel framework document which sets out the principles of managing CJD incidents, and also

describes the risk assessment models that underpin the risk management of surgical and blood incidents.

Appendix 1

Surgical procedures regarded as High Risk Posterior Segment Eye Surgery

Orbit (C01-C08)

C01 Excision of eye

C03 Insertion of prosthesis of eye

C04 Attention to prosthesis of eye

These orbital operations are only included if the surgery or implant is likely to come into contact with the optic nerve or retinal tissue (for example, evisceration of the eye and intra-orbital implant)

Operations on Optic Nerve (A29.1–A36.4)

A29.1 Excision of lesion of optic nerve

A30.1 Repair of optic nerve

A32.1 Decompression of optic nerve

A34.1 Exploration of optic nerve

A36.4 Radial Optic Neurotomy

Sclera and iris (C52-C65)

C54 Buckling operations for attachment of retina

Retina, other parts of eye and anaesthetics (C79-C90)

C79 Operations on vitreous body (only when this involves potential contact with the posterior hyaloid face). For example:

- Codes C7910 for vitrectomy via anterior approach and C7923 for intravitreal injections are specifically excluded as they are unlikely to come into contact with posterior hyaloid face
- Codes C7920 and C7922, which potentially could come into contact with hyaloid face, are included

C80 Operations on retinal membrane

C81 Photocoagulation of retina for detachment (only when the retina is handled directly)

C82 Destruction of lesion of retina (only when retina is handled directly). For example:

- Code C82.4 for insertion of radiotherapy plaques is specifically excluded

C83 Translocation of retina

C84 Other operations on retina

C85 Fixation of retina

C86 Other operations on eye

C88 Destruction of subretinal lesion

C89 Operations on posterior segment of eye

Appendix 2

Surgical procedures regarded as Low Risk Anterior Segment Eye Surgery

Orbit (C01-C08)

C02 Extirpation of lesion of orbit

C05 Plastic repair of orbit

C06 Incision of orbit

C08 Other operations on orbit

These orbital operations are only considered low risk if the surgery is unlikely to come into contact with the optic nerve (for example, drainage of orbit C0620 or retrobulbar injection C0840)

Eyebrow and eyelid (C09-C22)

C09 Replacement of canthal tendon

C10 Operations on eyebrow

C11 Operations on canthus

C12 Extirpation of lesion of eyelid

C13 Excision of redundant skin of eyelid

C14 Reconstruction of eyelid

C15 Correction of deformity of eyelid

C16 Other plastic repair of eyelid

C17 Other repair of eyelid

C18 Correction of ptosis of eyelid

C19 Incision of eyelid

C20 Protective suture of eyelid

C22 Other operations on eyelid

Lacrimal apparatus (C24-C29)

C24 Operations on lacrimal gland

C25 Connection between lacrimal apparatus and nose

C26 Other operations on lacrimal sac

C27 Operations on nasolacrimal duct

C29 Other operations on lacrimal apparatus

Muscles of eye (C31-C37)

C31 Combined operations on muscles of eye

C32 Recession of muscle of eye

C33 Resection of muscle of eye

C34 Partial division of tendon of muscle of eye

C35 Other adjustment to muscle of eye

C37 Other operations on muscle of eye

Conjunctiva and cornea (C39-C51)

C39 Extirpation of lesion of conjunctiva

C40 Repair of conjunctiva

C41 Incision of conjunctiva

C43 Other operations on conjunctiva

C45 Extirpation of lesion of cornea

C46 Plastic operations on cornea

C47 Closure of cornea

C48 Removal of foreign body from cornea

C49 Incision of cornea

C51 Other operations on cornea

Sclera and iris (C52-C65)

C52 Excision of sclera

C53 Extirpation of lesion of sclera

C55 Incision of sclera

C57 Other operations on sclera

C59 Excision of iris

C60 Filtering operations on iris

C61 Other operations on trabecular meshwork of eye

C62 Incision of iris

C64 Other operations on iris

C65 Operations following glaucoma surgery

Anterior chamber of eye and lens (C66-C77)

C66 Extirpation of ciliary body

C67 Other operations on ciliary body

C69 Other operations on anterior chamber of eye

C71 Extracapsular extraction of lens

C72 Intracapsular extraction of lens

C73 Incision of capsule of lens

C74 Other extraction of lens

C75 Prosthesis of lens

C77 Other operations on lens

Appendix 3

Guidance for the cleaning and disinfection (decontamination) of rigid contact lenses and ophthalmic medical devices which come into contact with the outer surface of the eye

1. The lens or device should be decontaminated immediately after contact with the eye surface. It should not be allowed to dry at this stage.

2. It should be rinsed in Water for Irrigation BP for not less than 30 sec.

3. It should then be cleaned on all surfaces with a liquid soap or detergent, then rinsed in Water for Irrigation BP for a further 30 sec.

4. The lens or device should then be immersed in a freshly-prepared solution of sodium hypochlorite providing 10,000ppm of available chlorine for 10 min.

5. It should then be rinsed in three changes of Water for Irrigation BP for a total of not less than 10 min.

6. The device should then be shaken to remove excess water, dried with a disposable tissue, and stored dry in a suitable container.

7. Any further measure (such as autoclaving) can then be carried out, if this is necessary and if the device is designed to withstand such a process. Otherwise, it is ready for immediate re-use.

8. Other chemical agents should not be used unless the device manufacturer advises against the use of sodium hypochlorite. However, agents or procedures capable of binding proteins to surfaces (e.g. isopropyl alcohol, glutaraldehyde, autoclaving) should never be used, unless devices are first decontaminated according the above protocol.

9. The procedure described above is suitable for the great majority of devices manufactured from PMMA, glass or non-ferrous metals. Where other materials are used, the manufacturer's advice should be sought.

Notes on steps 1-6

1. If circumstances do not permit the immediate decontamination of a contact lens or device, it should be immersed in Water for Irrigation BP contained in a disposable galley-pot, and decontaminated as soon as possible thereafter.

2. Most medical devices and instruments are decontaminated with the use of potable (drinking) water. However, this has not been recommended for contact lenses and ophthalmic instruments that come into contact with the ocular surface. This is because of the risk of contamination with *Acanthamoeba* spp. and is in line with the advice given to contact lens wearers, namely never to rinse their lenses or lens cases in tap water, and to avoid swimming and showering while wearing their lenses. The argument that rising mains water (as opposed to water from storage tanks) should be safe is not sustainable as it has been shown that rising mains pipework can become colonised by *Acanthamoeba* spp. even a short distance from its source. Moreover, in the clinical situation most people are unaware of the source of the water available to them at their workstations or in preparation rooms, or its distance from the mains supply. For these reasons, the use of tap water has not been recommended in this guidance.

3. The type of liquid soap or detergent is not specified. Unless the manufacturer publishes guidance, the advice of the local Sterile Services Department should be sought. Household detergents such as washing up liquid, and surgical scrub solutions, should not be used.

4. The sodium hypochlorite solution should be prepared immediately before the episode of decontamination. Such solutions are unstable and the concentration of available chlorine diminishes with time, especially in open containers. A recommended alternative to sodium hypochlorite solutions is NaDCC (sodium dichloroisocyanurate) which is available as tablets which are mixed just before use with a dedicated diluent or with Water for Irrigation BP. NaDCC, like sodium hypochlorite, is a source of hypochlorous acid and hence of available chlorine, and is widely used in healthcare environments; for example, dilutions giving 10,000 ppm available chlorine are recommended for the decontamination of blood spillages.

   The solution should be placed in a disposable plastic galley pot or similar disposable container. This should have a volume of not less than 50ml. (In the case of certain devices that cannot be wholly immersed, that part which comes into contact with the ocular surface must be so treated; the same consideration applies to Steps 2, 3 and 5.)

5. Starch iodide paper can be used to test the final rinse water. In the presence of residual hypochlorite or chlorine, the paper that is initially white will turn purple.

6. The lens or device will often have its own dedicated case for dry storage, but if not, a suitable case will have to be procured.

Appendix 4

Single-use instrumentation in ophthalmology

- The quality and performance of single-use instruments (SUI) should be equivalent to those of reusable instruments with appropriate procurement, quality control and audit mechanisms in place

- For reusable instruments there is an internal quality control, with instruments noted as faulty being either repaired or returned to the manufacturer. A similar process needs to be put in place for any SUI that is purchased

- A CE mark is not necessarily a mark of quality of instruments, and quality control of sub-contractors is often difficult when the number of instruments increases

- Manufacturers need to be encouraged to continue to produce high quality SUIs

- National contracts with manufacturers should be developed

- Quality control mechanisms for SUIs need to be developed which account for procurement, manufacturing and packaging. Evidence of this quality control must be clear, transparent and easily available to any individual using the SUIs

- A central reporting mechanism is to be encouraged to share information regarding the quality of instruments and to publicise this information nationally. This could be formally done through the Royal College of Ophthalmologists or via a website where the quality of instruments is constantly updated

- When considering the cost effectiveness of SUIs, appropriate costing is required not only for the purchase of the instruments but also their disposal. In addition, the potential cost savings of provision of reusable instruments and their subsequent decontamination and tracking should be taken into account

Appendix 5

List of members of the ACDP TSE Working Group Ophthalmology subgroup

Name	Role
Mr Ian Pearce (Chairman)	Consultant Ophthalmologist, Royal Liverpool University Hospital
Professor John Armitage	Professorial Research Fellow and Director of Tissue Banking, Bristol Eye Hospital
Professor Roger Buckley	Professor of Ocular Medicine, Anglia Ruskin University
Ms Pat Cattini	Infection Control Specialist, Royal Brompton Hospital
Ms Cecilia Fenerty	Consultant Ophthalmologist, Manchester Royal Eye Hospital
Mr Allan Hidderley	Medicines and Healthcare Products Regulatory Agency
Mr Ken Holmes	Northumberland and Tyne and Wear Mental Health Trust
Professor James Ironside	Professor of Clinical Neuropathology, University of Edinburgh Head of the Neuropathology Laboratories, National CJD Surveillance Unit
Professor Don Jeffries	Chair of the ACDP TSE Working Group
Mr Stephen Kaye	Consultant Ophthalmologist, Royal Liverpool University Hospital
Professor John Lawrenson	Professor of Optometry, City University, London
Mr Raymond Lobo	Associate Specialist in Ophthalmology, University College Hospital, London
Ms Gwyneth Morgan	Member of the College of Optometry
Mr Andrew Morrell	Consultant Ophthalmologist, St. James's University Hospital, Leeds
Mr Richard Newsom	Consultant Ophthalmologist, Southampton University Hospital

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Dr Mike Painter	Chair, Engineering and Science Advisory Committee into the decontamination of surgical instruments including Prion Removal
Mr David Pryer	Chair, CJD Incidents Panel
Professor Ian Rennie	Consultant Ophthalmologist, Royal Hallamshire Hospital, Sheffield
Dr Geoff Ridgway	Consultant Microbiologist Department of Health Senior Medical Officer
Professor Peter Shah	Consultant Ophthalmologist, Birmingham and Midland Eye Centre
Ms Jackie Shipley	Senior Theatre Nurse, Royal Liverpool University Hospital
Mr Alun Tomkinson	Consultant ENT Surgeon, University Hospital of Wales
Mr Barrie White	Consultant Neurosurgeon, Queen's Medical Centre, Nottingham

ANNEX M

MANAGING vCJD RISK IN GENERAL SURGERY AND LIVER TRANSPLANTATION

CONTENTS

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Introduction

M1. This guidance aims to provide practical advice for handling instruments that come into contact with medium infectivity tissues, involved in liver transplants and general surgical procedures, in order to reduce risk of vCJD transmission. It applies to all patients with or at increased risk of vCJD undergoing these procedures. The guidance has been produced by the Surgical Subgroup (membership list included as Appendix 1 of this document) of the ACDP TSE Risk Management Sub Group. It has been written in response to clinical concerns raised by both general and liver transplant surgeons.

M2. There is no evidence to suggest that vCJD is spread from person-to-person by close contact. However, it is known that transmission can occur, in specific situations, associated with medical interventions causing iatrogenic infections. Due to the possibility of iatrogenic transmission of vCJD, precautions need to be taken for certain procedures in healthcare to reduce the potential risk of transmission.

M3. The scientific rationale underlying this guidance is provided in Appendix 2.

Scope of this guidance

Type of tissue/surgery

M4. The potential risk of iatrogenic transmission of vCJD during a surgical or invasive diagnostic procedure is dependent on the level of tissue infectivity and the nature of the procedure itself. This guidance applies to medium infectivity tissue likely to be encountered in general surgical procedures and liver transplantation. These include:

- gut-associated lymphoid tissue
- lymph nodes and other organised lymphoid tissues containing follicular structures
- appendix
- spleen

- thymus
- tonsil

This guidance applies to surgical procedures where instruments come into contact with the cut surface of such tissues, for example operations involving the large and small bowel, the porta hepatis and axillary or cervical lymph nodes. It does not apply to procedures where only lymphatic channels are cut. See Annex A1 for further information on tissue infectivity.

M5. Olfactory epithelium and spinal ganglia are **not** included in this Annex as these tissues are not usually encountered in general or liver transplant surgery. Refer to Table 4d (Part 4) for guidance on the handling of instruments which may come into contact with these tissues.

Patient groups

M6. This guidance applies to:

- Patients who have been identified as being at increased risk of vCJD as defined in Table 4a (Part 4);
- Symptomatic patients with probable or definite vCJD.

It does not relate to patients with or at increased risk of, other prion diseases such as familial CJD and sporadic or iatrogenic CJD. For guidance on handling instruments used on these patient groups see Table 4c (Part 4).

M7. Annex J of the ACDP TSE Risk Management Sub Group guidance recommends that all patients about to undergo any surgery or endoscopy should be asked if they have ever been notified that they are at increased risk of vCJD. Annex J recommends that more detailed risk assessment questions should be asked of those patients who are undergoing high risk procedures. This Annex M applies to any patients presenting for general surgery and liver transplantation identified as at increased risk of vCJD through the initial question ‘have you ever been notified that you are at increased risk of CJD or vCJD for public health purposes’ only. These patients should not be asked any additional screening questions.

Surgical management

Elective surgery

M8. Any patient to whom this guidance applies should be identified at pre-surgical assessment. When any such patient has been identified, thought should be given to minimising the risks and costs involved in the planned surgical procedure. Communication with relevant individuals should be undertaken and this should include a discussion on the choice of instrumentation. For example, instruments could be streamed (see M9 for more detail) or single use (i.e. disposable) instruments could be procured.

Note: The quality of any alternative instruments should, however, be no less than those which would normally be used.

Streaming instruments

M9. Instruments may be streamed into those for incineration/quarantine or those that may be reprocessed. Instruments that have been in direct contact with the cut surface of medium infectivity tissues (see M4 above) should be regarded as potentially contaminated with the TSE agent. If possible, they should be separated from other instruments that have only come into contact with the external surface of medium or low infectivity tissues. Such instruments should either be incinerated after use or quarantined for re-use exclusively on the same patient. Instruments that have not been in direct contact with the cut surface of medium infectivity tissues may be reprocessed. Staff should liaise with the local sterile services provider to ensure that quarantined instruments are appropriately labelled and stored and also to ensure that destroyed instruments are replaced. The detail of how this is achieved will depend on local circumstances; the final decision rests with the local Infection Control Team.

Staffing levels

M10. Consideration should be given to increasing staffing, for example having two scrub nurses present to help identify and manage instruments that have not come into contact with the cut surface of lymph nodes. The role of one of the scrub nurses would be to manage the instruments which have been in contact with the cut surface of lymph nodes. A local policy should be in place to clarify these roles.

Emergency surgery

M11. In emergency surgery performed on a patient who has been notified they are at increased risk of vCJD, single use disposable instruments should be employed where possible. It is important that these instruments are of appropriate quality to deliver safe care. If the instruments used were not designed for single use, they should be incinerated following use.

General

M12. All instruments should be kept moist prior to being sent for conventional decontamination and reprocessing. There are a variety of methods, for example gels, sprays and use of wet towels, that could be applied to keep instruments moist; the choice of the exact method used rests with the local Infection Control Team following local risk assessment.

M13. Instruments quarantined may, following conventional decontamination, be made available for reuse exclusively on the same patient. The instrument set should be reprocessed through the sterile services provider in the usual manner. No special precautions are necessary because of the high dilution factor involved in the washer/disinfection process.

Equipment

M14. For high cost equipment (e.g. some complex retractors), where it is feasible, efforts should be taken to protect the retractor by using physical barriers, for

example sheaths and impervious drapes. In cases where only part of the instrument has come into contact with the cut surface of medium infectivity tissue, where possible, that specific instrument component should be discarded or quarantined for reuse exclusively on the same patient.

M15. The risk from ultrasonic dissectors or division devices used during these procedures is negligible.

Potential for the future

M16. This Annex will be regularly reviewed in the light of new developments in the areas of TSEs. In particular, developments in decontamination, single instrument labelling to enable tracking, and the possibility of developing instruments using materials (e.g. glass and plastic) to which TSEs do not adhere well will be considered.

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Appendix 1

List of members of the ACDP TSE Risk Management Sub Group's Surgical subgroup

Name	Role
Dr Adam Fraise (Chairman)	Consultant Microbiologist, University Hospital Birmingham NHS Foundation Trust
Professor James Ironside	Professor of Clinical Neuropathology, University of Edinburgh Head of the Neuropathology Laboratories, National CJD Surveillance Unit
Professor Don Jeffries	The Late Chair of the ACDP TSE Risk Management Sub Group
Mr Simon Bramhall	Consultant Hepato-pancreato-biliary & Liver Transplant Surgeon, University Hospital Birmingham NHS Foundation Trust
Mr John Forsythe	Clinical director of the Transplant Unit at the Royal Infirmary of Edinburgh Chair of the UK Advisory Committee on the Safety of Blood, Tissues & Organs
Professor John Lumley	General surgeon (retired) Member of the CJD Incidents Panel
Mr Thomas Groot-Wassink	Gastrointestinal surgeon, Ipswich Hospital NHS Trust Member of the Association of Surgeons of Great Britain and Ireland
Dr Miles Allison	Consultant Gastroenterologist, Royal Gwent Hospital, South Wales Member of the CJD Incidents Panel

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Appendix 2

Scientific rationale

A1. A number of current issues, including the epidemiology of vCJD and distribution of prion proteins in tissues, were considered whilst formulating these guidelines. These include:

- The prevalence of asymptomatic infection with vCJD in the UK population is uncertain; however, a figure of around 1 in 2,000 is estimated on the basis of current evidence. The number of clinical cases of vCJD to date is relatively small and all probable and definite cases have occurred in individuals who have a MM genotype at codon 129 in the prion protein gene. There is a possibility of further waves of cases in other genetic subgroups; it has been suggested that those patients with MV and VV *PRNP* codon 129 genotypes may have longer incubation periods than MM genotypes and that vCJD cases in these subgroups may yet be seen.
- vCJD diagnostics are difficult. No antibody response occurs following infection and no PCR-based test is available. At present it is not possible to screen for vCJD in asymptomatic individuals, but this is an area of active research.
- TSEs are resistant to conventional forms of decontamination. Procedures have been advocated in decontamination guidelines; however these are not completely suitable for use on all surgical instruments. Activity against prions has been claimed for some enzymes and detergents. These have been shown to work however they are difficult to implement in the NHS in a safe and practical way.
- vCJD has a wider distribution of tissue infectivity than other human TSEs. Infectivity in lymphoid tissue is present before the onset of neurological symptoms, but without a reliable screening method it is impossible to identify asymptomatic infected individuals. The incubation period for vCJD is unknown, but is estimated to be a period of years. Thus, there is the potential

for individuals to be infective and transmit the infection to others (via blood or surgical instruments) before being diagnosed with clinical vCJD themselves.

- It seems likely that exposure to vCJD infectivity will be greater from the cut surfaces of lymph nodes than the external surface or lymphatic channels.
- There have been no known cases of vCJD transmission via surgical instruments and no proven transmission of vCJD has occurred via instruments used on gut or lymph nodes; however, there is difficulty in identifying if transmission has occurred by this route through epidemiological studies, primarily because of the long incubation period in vCJD.

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The Royal College of Ophthalmologists

In conjunction with the Advisory Committee on Dangerous Pathogens
TSE Working Group

CJD Guidance for Ophthalmologists

Creutzfeldt-Jakob Disease (CJD) is an invariably fatal human disease caused by a pathological accumulation in the brain of an aberrant form of prion protein (PrP^{Sc}). Sporadic CJD (sCJD) is the most commonly encountered form of the disease with an incidence of 1 case per million, thus giving approximately 60 new cases per year in the UK. Patients with sCJD are mainly over 60 years of age and as such come into contact with ophthalmologists through a range of unrelated ophthalmic conditions or because of visual symptoms caused by their condition.

In 1996, a new form of CJD, now known as variant CJD, was identified in the UK. Epidemiological evidence linked the emergence of this disease with the large outbreak of bovine spongiform encephalopathy (BSE) in UK cattle; subsequent experimental studies found that the transmissible agents in BSE and vCJD have very similar biological properties, distinct from those of sporadic CJD. Case control studies have found that the most likely route of human exposure to the BSE agent was the consumption of BSE-contaminated beef products.

Although the majority of the human population of the UK may have been exposed to PrP^{Sc} by ingestion of contaminated beef products at some time until 1996, when controls were established, the precise prevalence of preclinical infection of vCJD in the UK is unknown. The most reliable evidence suggests a prevalence of up to approximately 1 in 4000 population (237 per million). Although the infective risk of these preclinical cases is uncertain there is the obvious potential for iatrogenic transmission in a significant number of cases.

Iatrogenic vCJD has been associated with blood transfusion. Treatment with human pituitary hormones, dura mater transplantation, contaminated neurosurgical instruments/EEG needles, and a single case of corneal transplantation from the US in 1974 have been associated with iatrogenic sCJD. There are no other known cases of ophthalmic surgery or diagnostic procedure having resulted in CJD transmission between patients.

Examination of ocular tissues from sCJD and vCJD cases have found high levels of PrP^{Sc} in the retina, comparable to levels with cerebral cortex, and lower levels in the optic nerve. However, no detectable levels of PrP^{Sc} have been found in cornea,

sclera, iris, lens, ciliary body vitreous or choroid. As prion proteins adhere strongly to materials including smooth metal surfaces and are not removed entirely by routine cleaning and autoclaving then there is the potential for iatrogenic transmission of PrP^{Sc} particularly during surgery involving the retina and optic nerve. Although the fact that PrP^{Sc} has not been found in other ocular tissues is reassuring, the **most likely case of** transmission of **CJD** through corneal transplantation suggests that practical precautions during diagnostic and surgical procedures are advisable to reduce the risk of iatrogenic transmission.

Previously, several sources of guidance have been produced to reduce the risk of iatrogenic CJD transmission in ophthalmic care by the Medical Devices Agency, the College of Optometrists, the Association of British Dispensing Opticians, the Royal College of Ophthalmologists and the National Institute for Health and Clinical Excellence (NICE).

The Advisory Committee for Dangerous Pathogens (ACDP) set up a working sub-group to specifically advise on CJD management in Ophthalmology. The membership of this working group consisted of ophthalmologists, optometrists, microbiologists, virologists and many other expert members reviewing and assessing the available evidence and existing guidance of CJD iatrogenic risk in ophthalmology. The purpose of this latest document is to consolidate and update the available guidance and offer pragmatic solutions to aid implementation of such guidance in a single source document. The guidance can be found at: (http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_104848.pdf)

A key aspect of the guidance was to assess the relative tissue infectivity risk status for anterior and posterior segment tissues. Previous guidance from ACDP had stratified tissue infectivity risk in to high (posterior eye), medium (cornea and anterior eye) and low (other ocular tissues). There is little controversy that posterior segment tissue should be considered as high risk tissue for CJD infectivity and robust adherence to advice on high risk tissue should be promoted. However, the working group agreed unanimously that anterior segment tissue should be effectively down graded to low infectivity risk. In essence, we now have only 2 infectivity risk states (high – for posterior segment tissue and low – for everything else). A similar down grading was recently introduced by the Australian Department of Health in December 2007. This grading now accords with the WHO *Guidelines on tissue infectivity distribution in transmissible spongiform encephalopathies* (**2010**), which places retina and optic nerve in the high-infectivity category and groups cornea with the lower-infectivity tissues.

The latest guidance helps clarify some key issues as to which surgery constitutes anterior low risk surgery and which should be considered high risk posterior segment surgery for purposes of iatrogenic CJD transmission. In addition, there are sections covering pre-operative assessment, surgical management of known cases of CJD or patients with increased risk of CJD, ocular tissue transplantation and management of CJD incidents within an ophthalmic unit (approximately 10 ophthalmic units per year in UK).

A potential contentious area within the guidance is with respect to cleaning/disinfection of ophthalmic lenses and devices. The generic advice includes disinfection steps to reduce significantly the problem of cross infection by conventional organisms such as viruses and bacteria, and thorough washing steps to reduce the level of residual protein and possible prion infectivity. The proposed regime is much more involved than that presently practiced in the majority of UK ophthalmic units but is considered as an effective method for reducing iatrogenic transmission of these organisms and prion protein. Due to the complexity of the regime in busy outpatient clinics several pragmatic solutions are identified to aid its implementation.

We hope that this latest guidance is accepted by colleagues as a document to clarify many confusing aspects of risk reduction of iatrogenic CJD transmission and aid local implementation.

We would encourage ophthalmic units to work closely with local infection control and decontamination units to assess their practices to reduce the risk of iatrogenic transmission of CJD without compromising ophthalmic care to their patients.

The guidance given in Annex L is a distillation of the views of a multidisciplinary expert advisory group. This guidance is however advisory. Should individual units take the view that the measures in Annex 3 are impractical for whatever reason, then they are strongly advised to seek the advice of their Infection Control Advisors and draw up a written local policy that is both practical and likely to be effective. The use of either Appendix 3 or the local policy should be audited on a regular basis to ensure compliance and hence safety, without compromising care of ophthalmic patients.

Mr Ian Pearce
Chair of ACDP TSE Ophthalmic Sub-Group

Mr Graham Kirkby
Chair of Professional Standards, RCOphth

Prof Don Jeffries
Chair of ACDP TSE Working Group

December 2010

Funeral arrangements after a CJD* death

Answers to some commonly asked questions

Are there any risks to relatives in viewing the body of a patient who has died with CJD?
There is no evidence that CJD can be passed from one person to another by contact with the skin or hair. Therefore, the body bag can be opened to allow relatives to view the body, and, if they wish, have contact with the deceased. The Department of Health (DH) and the Health and Safety Executive (HSE) have both issued advice on this important matter (see link at the end of this guidance note).

If an autopsy has been performed are there any additional risks to viewing the body of a patient who has died of CJD?
No, as above, the body bag can be opened to allow relatives to view the body, and, if they wish, have contact with the deceased, with no additional risk to either staff or relatives.

Are there any risks to relatives in dressing the body and washing the hair of a patient who has died of CJD?
As above, there is no evidence that CJD can be passed from one person to another by contact with the skin or hair. Therefore, the body bag can be opened to allow relatives to dress the body and wash the hair.

If an autopsy has been performed are there any additional risks to dressing the body and washing the hair of a patient who has died of CJD?
If an autopsy has been performed, dressing of the body and washing of the hair may be performed by relatives under the supervision of mortuary staff or a funeral director, using standard infection control measures to minimise risk.

Are there any risks involved in transporting the body of a patient who has died with CJD?
Precautions are required for the transport of people who have died with CJD. The body should be transported in a body bag to protect against accidental seepage of body fluids following death.

Following a CJD death, can the body be transported within the UK or abroad?
No additional precautions are needed for transporting the body within the UK.

However, 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 carrier, which should be discussed on a case-by-case basis.

Are special burial or cremation arrangements required for a patient who has died with CJD?
No special arrangements are needed for burial or cremation of a patient with known or suspected CJD.

What happens if I encounter problems with the funeral directors and others regarding funeral arrangements following a CJD death?
We are aware that some problems have been encountered in the past with funeral directors and others misunderstanding the risks posed from a body of a patient who has died with CJD. We appreciate that this can be very upsetting and we hope the information here clarifies the situation. In addition, a joint effort has been made by the Health and Safety Executive, the CJD Support Network and the Department of Health's ACDP TSE Working Group to raise awareness of the guidance issued by HSE and DH regarding funeral arrangements. Funeral directors may find the following guidance document helpful:
http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/tseguidance_annexh.pdf

*This guidance is intended to apply to all forms of human transmissible spongiform encephalopathy or prion disease

Final

Alert to Urological Surgeons

TRANSRECTAL PROSTATIC BIOPSY IN MEN AT RISK OF VARIANT CJD

It has come to the attention of the Advisory Committee on Dangerous Pathogens' TSE Working Group and the CJD Incidents Panel that some transrectal prostatic biopsies are undertaken by means of single use needles passed **through the internal lumens** of reusable ultrasound probes (e.g. BK Medical Triplane, Biplane or Endfire).

The ACDP TSE Working Group categorises surgical and other invasive procedures according to their potential for onward transmission of tissue contaminated with abnormal prion protein, the putative infective agent in variant Creutzfeldt Jakob disease (vCJD)[1]. Lymphoid aggregates occur in rectal mucosa and submucosa, and have been shown to be contaminated with abnormal prion protein in cases of vCJD. There is therefore a potential risk of vCJD cross-infection during transrectal prostatic biopsy if reusable equipment is employed for this procedure on patients at risk of vCJD, because there is no decontamination method that reliably eliminates or destroys abnormal prion protein.

It is understood that most transrectal prostatic biopsies are undertaken by means of single use needle devices guided by an **adjacent** ultrasound probe. As the biopsy instruments are single use, there is no reason why such procedures would carry a potential risk of cross-infection.

Therefore the ACDP TSE Working Group and CJD Incidents Panel advise the following:

Patients at risk of vCJD[2] requiring transrectal prostatic biopsy should have the procedure performed by means of single use equipment that runs alongside (rather than through) the ultrasound probe. Where a unit does not have such equipment and intends to carry out a biopsy procedure on a patient at risk of vCJD, their options are as follows:

- **To refer the patient to a unit offering the alternative technique that does not pose a risk of contaminating the internal channels with traces of biopsy tissue**
- **To borrow the alternative equipment from another unit**
- **To undertake the procedure with equipment that has internal biopsy channels and then quarantine the reusable components of that equipment after decontamination. It must be accepted that this equipment would be unlikely to return to general use, except for dedicated re-use in the same patient.**

Dr Miles C Allison, Gastroenterology Representative, CJD Incidents Panel and ACDP TSE Working Group Endoscopy Subgroup
Professor Don Jeffries, Chairman of the ACDP TSE Working Group
Mr David Pryer, Chairman of the CJD Incidents Panel

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[1] http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/

[2] The following patient groups have been notified of their increased risk of subclinical vCJD infection:

- People who have received blood from someone who went on to develop vCJD
- People who have given blood to someone who went on to develop vCJD
- People who have received blood from someone who has also given blood to a patient who went on to develop vCJD
- People who have had surgery using instruments that had been used on someone who developed vCJD
- People who have received an organ or tissue from a donor infected with vCJD or at increased risk of vCJD
- People who have been treated with certain UK sourced plasma products between 1980 and 2001

It is important to note that new patient groups may be notified in the future of their increased risk of vCJD.

Advisory Committee on Dangerous Pathogens
Transmissible spongiform encephalopathy agents: safe working and the prevention of infection

Frequently asked questions

Please note, in the following section the "Transmissible Spongiform Encephalopathy agents: safe working and the prevention of infection" guidelines will be referred to as the TSE guidance.

My patient has a history of blood transfusion. Should my patient be considered at increased risk of CJD and/or vCJD?

A number of patients have been identified as “at increased risk” of vCJD because of their transfusion history. Around 140 individuals have a direct link/association with someone who developed vCJD, through the donation of blood to or receipt of blood from them; these individuals have been informed about this risk. In addition, a larger group of individuals are defined as being at increased risk because they have received blood or blood components from a large number of blood donors during the course of their treatment. Current risk assessments ([1]Department of Health, 2013) estimate that where an individual has been exposed to around 300 or more blood donors since January 1990, public health precautions, including those for surgical and endoscopic instruments, should be followed. It is acknowledged that it may not be easy to establish from an individual’s records exactly how many donors have provided blood or blood products for an individual so the 300 figure should be used as a guide not an exact figure to indicate whether they should be considered at increased risk.

My patient has told me that he/she has received large quantities of donated blood. Should my patient be considered at increased risk of CJD and/or vCJD?
A number of patients have been identified as “at increased risk” of CJD or vCJD including people who have been designated because of their transfusion history. This definition only concerns those who have received blood or blood components from 300 or more donors since January 1990. It is acknowledged that it may not be

[1] https://www.gov.uk/government/publications/vcjd-and-transfusion-of-blood-components-updated-risk-assessment

easy to establish from an individual's records exactly how much blood an individual has received so the 300 figure should be used as a guide not an exact figure to indicate whether they should be considered at increased risk.

My patient has told me that he/she has received hormone treatment. Should my patient be considered at increased risk of CJD and/or vCJD?

Only recipients of human pituitary-derived hormone treatment, for example with growth hormone or gonadotrophin, should be regarded as at increased risk of sporadic CJD (see details in Table 4a of Part 4 of the TSE guidance). Recipients of synthetic hormone treatment are not at risk of either sporadic CJD or vCJD.

The date and place of treatment is important in determining whether the hormone was human-derived or synthetic. In the UK, the use of human pituitary-derived gonadotrophin was discontinued in 1973 and the use of human pituitary-derived growth hormone was discontinued in 1985. However human-derived products may have continued to be used in other countries after these dates.

As it is unlikely that human pituitary-derived growth hormone would have contained the vCJD infectious agent, recipients should not be considered at increased risk of vCJD.

My patient received a human-derived dura mater graft – should he/she be considered at increased risk of all forms of CJD including vCJD?

Patients who received a graft of human-derived dura mater before August 1992 (when the use of these grafts was discontinued in the UK) are at increased risk of sporadic CJD, but not vCJD.

This difference in risk has implications for patient management, in particular gastrointestinal endoscopy, due to the difference in tissue infectivities in the gastrointestinal tract in CJD and vCJD cases. Annex F of the TSE guidance gives advice on endoscopes and CJD/vCJD infection prevention and control.

How can I ensure all my patients are effectively assessed before surgery to identify patients with, or at increased risk of, CJD/vCJD?

Guidance on assessment to be carried before surgery or endoscopy, to identify patients with or at increased risk of CJD/vCJD, can be found in Annex J of the TSE guidance.

This advises that all patients coming in for any surgery or endoscopy should be asked if they have been informed that they are at increased risk of CJD/vCJD.

Additionally, those patients coming in for high risk surgical or endoscopy procedures (neurosurgery, neuroendoscopy or posterior ophthalmic surgery) should be asked specific questions to determine whether they are at increased risk of CJD/vCJD.

Where can I find advice on endoscopes and CJD/vCJD infection prevention and control?

Advice on endoscopes and CJD/vCJD infection prevention and control is given in Annex F of the TSE guidance and the accompanying Consensus Statement between the British Society of Gastroenterology Decontamination Working Group and the ACDP TSE Working Group Endoscopy and vCJD Subgroup. This Annex contains a list of endoscopic procedures and their categorisation as 'invasive' or 'non-invasive'. This categorisation has implications for the consequent management of the instruments used during the procedure.

Please note: if a patient has, or is at increased risk of, sporadic or genetic CJD, special precautions do not need to be taken for gastrointestinal endoscopy. Special precautions only need to be taken for gastrointestinal endoscopy for patients with, or at increased risk of, vCJD. This is because of the difference in tissue infectivities in the gastrointestinal tract in CJD and vCJD cases.

Where can I find advice on dialysis and CJD/vCJD infection prevention and control?

Guidance on dialysis and CJD/vCJD will be included in the updated Annex G of the TSE guidance that will be published in due course. Please check back to the TSE Guidelines webpage to see if the guidance has been published or alternatively contact the secretariat, asking for an email alert when this annex is published. If you have an urgent query then please contact the ACDP Secretariat.

Where can I find advice on ophthalmology and CJD/vCJD infection prevention and control?

There are a number of guidance documents issued by professional bodies that give advice on ophthalmology and CJD/vCJD.

Guidance from the ACDP TSE Working Group on ophthalmology and CJD/vCJD will be published later in 2009 as a new annex of the TSE guidance. Please check back to the TSE Guidelines webpage to see if the guidance has been published or alternatively contact the secretariat, asking for an email alert when this annex is published. If you have an urgent query then please contact the ACDP Secretariat.

Where can I find advice on dentistry and CJD/vCJD infection prevention and control?

The Chief Dental Officer has written twice to dentists on the issue of dental treatment of patients with, or at risk of, CJD. The key points are as follows:

Letter from Chief Dental Officer to dentists in 2005:
http://www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Dearcolleagueletters/DH_4102752

This letter states that the clinical care – including dental care – of patients with or at risk of CJD/vCJD, should not be compromised in any way, and that patients are not refused routine dental treatment.

Letter from Chief Dental Officer to dentists in 2007:
http://www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Dearcolleagueletters/DH_074001

This letter clarifies the situation with regard to decontamination and re-use of instruments, especially those used in endodontic treatment, in the context of vCJD. It contains revised advice that dentists are expected to follow. Dentists are advised to ensure that:

- Endodontic reamers and files are treated as single use
- The highest standards of decontamination are observed for all dental instruments
- Manufacturers' decontamination instructions are followed for all instruments, and where instruments are difficult to clean, single use instruments should be used wherever possible

The CJD Incidents Panel also issued an advice note in 2006 on dental treatment on patients with, or at risk of, CJD/vCJD:
http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1211788871050

Where can I find advice on anaesthesia and CJD/vCJD infection prevention and control?

The Association of Anaesthetists of Great Britain and Ireland (AAGBI) have recently published an update to their 2002 guidance "Infection prevention and control in Anaesthesia" which includes a section on prion diseases. This guidance can be found here: http://www.aagbi.org/publications/guidelines/docs/infection_control_08.pdf

Where can I find advice on decontamination and CJD/vCJD?

Annex C of the TSE guidance provides advice on decontamination. This Annex is currently being updated by the ACDP TSE Working Group, and it is hoped that this updated Annex will be published shortly.

The Engineering and Science Advisory Committee into the decontamination of surgical instruments including prion removal (ESAC-Pr) published a report in 2006 entitled "The decontamination of surgical instruments with special attention to the removal of proteins: and inactivation of any contaminating human prions". This can be found here: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_072443

ESAC-Pr have also published a report on prion inactivating agents, written by their New Technologies Working Group. This can be found here: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_086805

It is important that, until the efficacy of products and technologies claiming to remove/inactivate prion protein from contaminated medical devices in laboratory and clinical practice is established fully against human prions, clinicians and laboratory managers should ensure that the current ACDP TSE guidelines are followed.

Advisory Committee on Dangerous Pathogens (ACDP)

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

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 2002
CSF:	cerebrospinal fluid
CWD:	chronic wasting disease
DEFRA:	Department for Environment, Food and Rural Affairs
DH:	Department of Health
ENT:	ear, nose and throat
FFI:	fatal familial insomnia
FSE:	feline spongiform encephalopathy
GSS:	Gerstmann Sträussler Scheinker disease
hGH:	human growth hormone
hPG:	human pituitary gonadotrophin
HSAC:	Health Services Advisory Committee
HSE:	Health and Safety Executive
MBM:	meat and bone meal
MHSWR:	Management of Health and Safety at Work Regulations 1999
nvCJD:	distinct variant of Creutzfeldt-Jakob disease first reported in March 1996
PPE:	Personal Protective Equipment
ppm:	parts per million
PrP:	prion protein
RIDDOR:	Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995
SBO:	specified bovine offal
SEAC:	Spongiform Encephalopathy Advisory Committee
SSD:	sterile services department
TME:	transmissible mink encephalopathy
TSE:	transmissible spongiform encephalopathy
UV:	ultraviolet radiation

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

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