CJD INCIDENTS PANEL

Management of possible exposure to CJD through medical procedures

A consultation paper

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Foreword

This document sets out proposals for managing incidents involving possible exposure to CJD in healthcare settings. Incidents arise when patients who are diagnosed or suspected of having CJD are found to have undergone a medical procedure at some time in the past. Other patients could be put at risk if CJD is transmitted through contaminated instruments and/or devices, blood or other tissues or organs donated by patients with CJD.

The CJD Incidents Panel is the expert committee set up by the Department of Health to advise Health Authorities and Trusts on how to manage these incidents. This document explains the basis on which the panel provides advice.

The risk of transmitting CJD through medical interventions is not fully understood, and this document has been prepared in the face of great scientific uncertainty. While there are many areas of doubt, this guidance has been able to draw on the work of the Spongiform Encephalopathy Advisory Committee (SEAC), the government's expert scientific committee on CJD and BSE.

The guidance particularly draws on two reports: 'Risk Assessment for Transmission of variant CJD via Surgical Instruments: A modelling approach and numerical scenarios (referred to in this guidance as the surgical risk assessment), and 'Assessment of the risk of exposure to variant CJD infectivity in blood and blood products' (referred to in this guidance as the blood risk assessment). The guidance also builds on the conclusions of an expert Peer Review Group that was set up by SEAC to assess the available data in this area. The risk assessment for blood and plasma derivatives requires further work and the framework document provides provisional guidance, based on the assessment currently available.

This is a working document and will be updated as new scientific evidence becomes available. It currently covers incidents involving surgery and blood donations. Future versions will also address tissue and organ donations and transplantation, as well as dental procedures carried out on patients who subsequently develop CJD.

This document sets out the reasoning behind the Incidents Panel's advice, and is intended to support health care professionals and trust managers involved in incidents.

The document is also being made available to others in the medical and allied professions and to anyone else with an interest. It is being published on the Department of Health's website at: http://www.doh.gov.uk/cjd/consultation

Executive summary

It is possible that variant and sporadic CJD may be transmitted on surgical instruments used on patients incubating the disease, or in blood, other tissues or organs donated by individuals incubating the disease. These risks are unknown, but current procedures for decontaminating surgical instruments between uses cannot be guaranteed to eliminate the abnormal prion proteins that are thought to be responsible for the transmission of CJD. In addition, while there is evidence that sporadic CJD is not transmitted in blood, less is known about variant CJD. Therefore transmission of variant CJD in blood cannot be ruled out.

The Department of Health has set up an expert advisory group to advise health authorities and trusts on managing incidents in which an invasive medical procedure has been carried out on someone who later develops CJD.

The panel includes bioethicists, lay members, and relevant experts, under the chair of a moral theologian. This document sets out a proposed framework for the Panel's advice, and will also inform health professionals and managers involved in these incidents.

Public health actions are needed as contaminated surgical instruments may transmit CJD to other patients. Public health actions are also needed in case blood transmits variant CJD.

There is a great deal of scientific uncertainty about the infectivity of different tissues (including blood) in people incubating CJD, and about the effects of decontaminating surgical instruments and of processing blood. This document sets out what is known about these factors, and shows how the Panel assesses the risk for different medical procedures.

The document also advises on identifying, investigating and managing these incidents. The Panel proposes four main courses of action:

1 Removing the instruments/blood products from use

This protects public health while the risks are being assessed. The Panel may advise that instruments are destroyed or that they are unlikely to pose a risk to the public and may be returned to use. The Panel will also advise on the removal from use of blood or plasma products donated by people who later develop CJD.

2 Setting up a confidential database of all possibly exposed people

The database would be used for the long-term follow up of individuals who could have been exposed to CJD through medical procedures. This database would be used to find out whether any exposed individuals go on to develop CJD themselves, so increasing our knowledge of these risks.

It is proposed that most people would not be informed about their possible exposure. This is because the average incubation period for CJD transmitted between people is unknown but could be well over 10 years; there is currently no reliable diagnostic test for people incubating the disease; there is no cure for this fatal disease; and the risks of transmitting CJD through medical procedures are very uncertain. Moreover, CJD is not thought to spread between people through normal social contact. Therefore, learning about one's exposure would be of doubtful benefit to individuals and could inflict psychological harm.

There is a strong argument that people should be able to choose whether or not they are told about their possible exposure. Therefore it is proposed that possibly exposed people are not asked for their informed consent before being recorded on this register. This is because such action would remove the choice of not being told about their exposure. Instead it is proposed that individuals who wish to know if they are on the database, and the details and significance of their exposure, should be able, after appropriate counselling, to obtain the information through their doctor.

3 Informing some individuals about their exposure to CJD

The exception to this would be a small sub group of possibly exposed people who the Panel considers to be at sufficient risk to warrant public health action. It is proposed that these people are contacted and informed about their exposure so that they can be advised not to donate blood or organs, and to contact their doctor if they required surgery in the future.

4 Providing publicity

The Panel proposes that publicity is provided to alert the public to the existence of the database and that information is provided on how someone could find out whether they are on the database, and how they can have their details removed if so desired.

Section 1: Introduction

Background

Creutzfeldt-Jakob disease

1.1 Creutzfeldt-Jakob disease (CJD) is a rare and fatal neurological condition that affects the nervous system. It is one of a group of transmissible disease known as the prion diseases or transmissible spongiform encephalopthies (TSEs). All types of CJD are associated with a conformational change in a protein called the 'prion protein'. The abnormal form of this protein accumulates in the brain in these disorders and results in the death of nerve cells.

1.2 The commonest form of CJD is sporadic CJD, which affects approximately one per million of the population per annum across the world, and accounts for around 85% of all cases of CJD. Around 60 cases of sporadic CJD are reported annually in the UK. The underlying cause of sporadic CJD is not known. Around 10% of cases occur as familial diseases (Familial CJD, Gerstmann-Sträussler-Scheinker syndrome and Fatal Familial Insomnia). These disorders are associated with mutations in the prion protein gene and are inherited as autosomal dominant conditions. Rarer forms of TSEs include acquired diseases such as Kuru (confined to the Fore tribe in Papua New Guinea), and iatrogenic CJD transmitted between people by medical and surgical procedures including injections with human pituitary hormones, dura mater (membrane covering the brain) grafts, and very rarely by neurosurgical instruments.

1.3 Variant CJD (vCJD) is a novel form of human TSE which was first recognised in 1996. This new disease is associated with the same transmissible agent that is responsible for Bovine Spongiform Encephalopathy (BSE). Experimental studies have shown that the BSE agent is not related to sporadic CJD. There have been over 100 confirmed or probable cases of variant CJD in the UK[a]. Variant CJD is thought to have resulted from the consumption of contaminated bovine food products. Most of the population of the UK has probably been exposed to BSE, and we do not know how many people have been infected but currently show no signs of neurological disease. Estimates range from a few hundred to many thousands. Variant CJD also differs from other human TSEs in that the transmissible agent accumulates outside the central nervous system in the lymphoid tissues throughout the body and in parts of the peripheral nervous system (see section 2).

Transmission of CJD

1.4 While there is no evidence that any type of CJD can spread between people through normal social contact, sporadic CJD has been transmitted between patients undergoing certain medical treatments. Transmission has followed neurosurgical procedures, corneal graft operations and treatment with hormones prepared from human pituitary glands. One of the reasons that transmission may occur is that prion proteins are resistant to normal methods of decontaminating surgical instruments.

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[a] On 3rd August 2001, 106 definite and probable cases of variant CJD had been reported to the CJD Surveillance Unit

1.5 Variant CJD has not yet been shown to be transmitted through surgical operations, or blood or tissue donations. However, it is a new disease, and there is no practical screening test to detect it during its (probably) long incubation period. This means that it may be too early to detect any cases that may have been transmitted between individuals.

Action to prevent transmission of CJD through healthcare

1.6 Guidance has been issued on what action should be taken to prevent CJD being transmitted from patients who have symptoms of CJD or who have a specific risk of developing CJD (**Annex 1**). Actions include destroying surgical instruments used on these patients[3] and not donating their blood, tissues or organs to other patients[4].

1.7 However, it is more difficult to prevent transmission of CJD from patients who are incubating the disease. This is relevant when patients diagnosed or suspected of having CJD are found to have undergone surgical procedures or donated blood, tissues or organs in the past.

1.8 For procedures performed some years ago, most of the risk from instruments contaminated with prion agents is likely to have already occurred. However, as prion agents resist standard decontamination procedures, it is possible that such instruments could continue to pose a risk to future patients.

1.9 This situation is difficult to manage as it may not be possible to identify which instruments were used in a particular operation carried out some time ago. To remove all possibly remaining risk one would need to destroy any instrument that might have been used on a patient with CJD. In practice this could leave surgical units unable to function.

1.10 Some people with CJD may have donated blood, tissues or organs before they developed symptoms. The long incubation period of CJD makes it likely that such donated tissues will have been used by the time the donors are diagnosed with CJD.

1.11 Action has been taken to reduce the risk of transmitting variant CJD through plasma derivatives such as clotting factors and immunoglobulins. Since 1998 the plasma used to make these products has been imported from countries with little or no BSE. Donors in these countries are highly unlikely to be incubating variant CJD.

1.12 Much remains to be discovered about the infectivity of different tissues and the effect of decontamination processes on prion proteins. As the risk of transmitting CJD in healthcare settings is unknown, a precautionary approach to the management of the possible risk is advisable. However, the unknown risk of acquiring CJD from medical procedures needs to be considered alongside the background risk to the UK population following exposure to BSE. The known risks and benefits inherent to surgery and other medical procedures must also be considered.

1.13 There are ethical and practical issues around informing people that they might have been put at risk. Some of these people may have a relatively high chance of being infected with CJD. They will need to be informed so that they do not themselves transmit the infection to other patients. Other people will have a smaller risk of acquiring the disease. For this group, information about possible exposure risks should be made available to those who want it. However, this information potentially brings with it a great burden, as CJD is a fatal disease for which there is as yet no diagnostic test and no cure.

Aims

1.14 This document provides a framework for managing incidents which arise when individuals have undergone medical procedures or have donated blood, tissues or organs and are subsequently diagnosed or suspected of having CJD. This framework has four main aims:

- To protect patients from the risk of acquiring CJD in healthcare settings.
- To ensure that those who might have been exposed are informed in a manner appropriate to their level of risk.
- To ensure that those who might have been exposed to lower levels of risk, while not being actively informed, are able to find out about their exposure if they so wish.
- To increase our knowledge about the risk of transmitting CJD in healthcare settings, to be better able to manage any risk.
- To ensure that the public is informed about possible risks of acquiring CJD through healthcare.

Purpose of document

1.15 The CJD Incidents Panel is an expert group set up by the Department of Health on behalf of all UK Health Authorities to advise Health Authorities (Health Boards in Scotland) and Trusts on how to manage possible exposures to CJD in healthcare settings. The Panel advises on incidents throughout the UK.

1.16 All incidents should be referred to the CJD Incidents Panel at the start of any investigation.

1.17 This document sets out the basis for decision making by the CJD Incidents Panel, and should be used by public health doctors, infection control teams, clinicians, trust managers and other professionals responding to local incidents.

1.18 This framework sets out what is known about the risk of transmitting CJD through invasive medical procedures including blood donation. It then describes how incidents should be identified and investigated, and the public health actions to be taken. The final section describes how public communication should be carried out.

1.19 Current scientific uncertainties mean that this framework will evolve, being revised as scientific research proceeds.

1.20 This guidance should be seen in the context of other policy and advice on preventing the spread of CJD in healthcare **(Annex 1)**.

Principles

1.21 Incidents should be managed according to the following principles:

- To protect patients from the risk of acquiring CJD in healthcare settings.
- To provide consistently high quality advice and information to people who may have been put at risk.
- To provide information to people who may have been put at risk while respecting where possible the wishes of those who do not want to be informed.
- To be open about the risk of acquiring CJD in healthcare settings and the scientific uncertainties surrounding this risk.
- To increase our knowledge about the risk of spreading CJD through medical procedures.
- To protect the confidentiality of infected patients and those at risk of acquiring CJD.
- To ensure that actions taken to protect the public health do not prejudice individual patient care.

Section 2: Supporting Evidence

Introduction

2.1 This section describes what is currently known about the risk of transmitting variant Creutzfeldt-Jakob Disease (CJD) or sporadic CJD through medical interventions. While some of our understanding is based on direct evidence on variant CJD or sporadic CJD in humans, more is known about how other Transmissible Spongiform Encephalopathies (TSEs) behave in animal models.

2.2 Little work has been carried out into tissue infectivity in familial or iatrogenic CJD. This guidance assumes that infectivity in these diseases resembles that found in sporadic CJD. Similarly, in the absence of any data to the contrary, other human TSEs are assumed to have the same infectivity pattern as sporadic CJD.

2.3 Broadly, four inter-relating factors determine whether the use of a surgical instrument is likely to transmit CJD infection between patients. These are:

- The infectivity of the tissues in the patient with CJD that come into contact with instruments.
- The amount of infectivity remaining on the instruments following decontamination.
- Which tissues in subsequent patients come into contact with the instruments.
- The susceptibility of subsequently exposed patients.

2.4 In a similar way, the likelihood of transmitting CJD through blood or tissue donation depends on the infectivity in the donated blood and other tissues; the amount of infectivity remaining after processing, the amount of blood or tissue that is transferred to the recipient patients; and the susceptibility of recipient patients.

2.5 A key element affecting the transmission of an infection is the relationship between the dose received and the 'response' to it – i.e. the chance of becoming infected. This guidance is based on a linear dose-response relationship, i.e. the chance of infection is proportional to the dosage received, with no lower threshold. This assumption has been endorsed by SEAC as a provisional working model and has been used for the basis of risk calculations.

Infectivity of tissues in variant CJD

2.6 There is a growing body of experimental evidence on which tissues contain PrP^{Sc} and which may transmit CJD. There is also epidemiological evidence on the transmission of CJD through medical procedures involving different tissues.

2.7 Most of the experimental research has been carried out using animal models and TSEs other than CJD. Only a small number of studies have examined the behaviour of CJD in humans. Because of this, the available evidence has been categorised according to its likely relevance to transmission of CJD in healthcare. Studies considered to be most relevant are those that have demonstrated infectivity in the tissues of patients with CJD. Studies considered to be least relevant include those that have detected infectivity in tissues of animals infected with TSEs such as scrapie (Table 1). This classification does not reflect the quality of the studies considered.

Table 1 Relevance of experimental evidence

Experimental evidence	Relevance of evidence
CJD in human tissue: infectivity demonstrated	A
CJD in humans: epidemiological evidence	B
CJD in human tissue, PrP^{Sc} detected	C
TSE in animal model, infectivity demonstrated	D

Infectivity in the brain and spinal cord

2.8 Brain tissue of patients who have died of variant CJD has the highest level of infectivity of all the tissues studied[5]. **A**

2.9 The brain and spinal cord tissue have also been found to have the highest levels of infectivity in studies conducted on scrapie-infected mice,[6]. The dura mater of scrapie-infected hamsters[7] has also been shown to transmit infection. **D**

2.10 Experiments performed on scrapie-infected mice indicate that abnormal prion protein in the brain and spinal cord appears later in the incubation period than in lymphoreticular tissue[8]. **D**

Infectivity in the eye

2.11 Recent research has detected PrP^{Sc} in the optic nerve and retina of a single patient with variant CJD . The amount of PrP^{Sc} in these tissues was equivalent to 2.5% and 25% respectively of the levels found in the brain. PrP^{Sc} was not detected in the sclera, vitreous humour, lens, aqueous humour, iris or cornea. The limitations of the detection methods used in this study mean that if PrP^{Sc} was present in these tissues, it was at levels less than 1/400 of that found in the brain. It is not known how levels of PrP^{Sc} relate to tissue infectivity. **C**

2.12 Studies on scrapie-infected hamsters indicate that infectivity levels in the optic nerve and retina are comparable with levels in the brain[10]. Lower levels of infectivity are present in the cornea, pigment epithelium/choroid and lens. This animal model experiment also suggested that infectivity is present in the brain and eye before the signs of disease. **D**

2.13 Experiments on hamsters infected with transmissible mink encephalopathy also indicate that the cornea is less infective than brain tissues[11]. This study did not demonstrate infectivity in the aqueous humour. **D**

2.14 PrP^{Sc} has been detected in eye tissues in experimental scrapie at a similar point in the incubation period as it is found in the brain[12]. **D**

Infectivity in the lymphoreticular system (LRS)

2.15 Recent research has found that the spleen and tonsil have similar levels of infectivity in variant CJD, and that these levels are 100 to 1,000 times lower than infectivity levels in the brain[5]. **A**

2.16 Other research has indicated that levels of PrP^{Sc} are higher in the tonsils than in other parts of the LRS[9]. **C** The relationship between the amount of PrP^{Sc} in tissues and infectivity is not clear.

2.17 The LRS is involved in the incubation period of variant CJD infection. PrP^{Sc} has been detected in the appendix of a patient eight months before symptoms of variant CJD developed[13]. **C**

2.18 The LRS continues to be involved during clinical disease, and PrP^{Sc} has been detected in the tonsil, spleen and lymph nodes of people who have died of variant CJD and in tonsilar biopsies of patients with symptomatic disease[14] . **C**

2.19 Infectivity has been detected in the LRS of scrapie-infected mice and sheep early in the incubation period[8 15]. Infectivity levels in the LRS of scrapie-infected mice have been found to be lower than in brain and spinal cord tissue.[6] **D**

Infectivity in other tissues

2.20 Studies on peripheral nerve tissue from four patients with variant CJD did not detect PrP^{Sc}. PrP^{Sc} has been detected in dorsal root ganglia and trigeminal ganglia in variant CJD[16]. **C**

2.21 Research on other peripheral tissues has detected low levels of PrP^{Sc} in the rectum, adrenal gland and thymus of a single patient with variant CJD. Levels of PrP^{Sc} in these tissues were about 1/50,000 of that found in brain tissue[9]. **C**

2.22 Infectivity has been demonstrated in the dental tissue of scrapie-infected hamsters that were in the clinical stage of the disease[17]. This experiment indicated that infectivity levels in the gingival and pulp tissues were lower than in the trigeminal ganglia. **D**

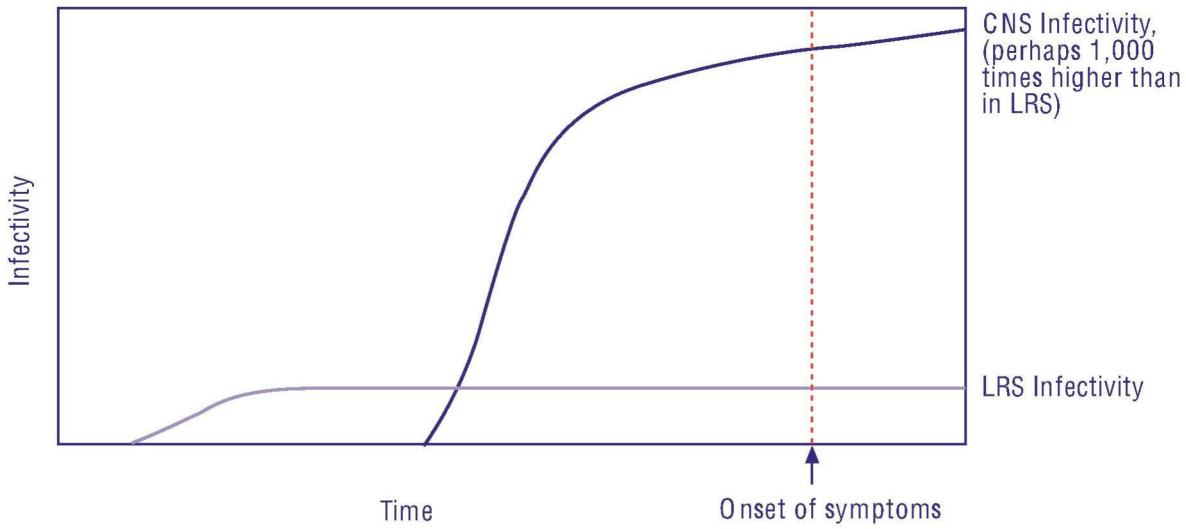
2.23 Other studies on scrapie-infected mice indicate that gingival tissues are infective, although experimental transmission was only achieved with difficulty.[18 19] **D**

Disease progression

2.24 The incubation period for variant CJD is not known, but the median incubation period could be between 10 and 30 years. For practical purposes, this is taken to be any time since BSE could have started in 1980. Extrapolating from animal models, the distribution of PrP^{Sc} and infectivity in variant CJD is expected to change as the infection progresses.

2.25 The expected time course for the changes in infectivity in different tissues in variant CJD is shown schematically in Figure 1.

Figure 1 Probable pattern of tissue infectivity in variant CJD, based on scrapie models



Route of transmission

2.26 Disease transmission depends not only how much infectivity is present in the tissue, but also on where in the recipient the tissue is deposited. Animal experiments indicate that the most efficient transmission route is directly into the brain (intracerebral inoculation)[20 21 22]. **D**

2.27 This guidance follows the assumptions made in the surgical risk assessment[1], that transmission of variant CJD via material deposited into brain, spinal cord or posterior eye is at least ten times more efficient than if similar material is deposited into any other site. The same assumption is made for sporadic CJD.

Conclusions on tissue infectivity in variant CJD

2.28 The infectivity levels in different tissues in variant CJD are uncertain. However, assumptions may be based on the limited amount of evidence that is available. This guidance builds on the infectivity assumptions used in the surgical risk assessment[1] endorsed by SEAC. These conclusions are described in Table 2. **[Dental tissues will be added at a later date].**

Table 2 Infectivity estimates in variant CJD

CNS

Infectivity within the CNS is low in the early incubation stage, but increases as disease develops[b]. Infectivity levels of 10^8 i/c ID_{50}/g may occur in the last 40% of the incubation period and increase to 10^9 i/c ID_{50}/g, or even 10^{10} i/c ID_{50}/g during clinical disease.

Eye

The retina and optic nerve are thought to have infectivity levels that could be as great as that found in brain tissue. Other parts of the eye (cornea, lens, conjunctiva) are thought to contain 10 to 10^2 times less infectivity than brain tissue.

Infectivity in the eye is believed to increase as disease develops, with the levels cited appearing in the last 40% of the incubation period. A further 10-fold increase may also occur in the final year before the onset of symptoms.

Lymphoreticular System (LRS)

From early in the incubation period until death, infectivity levels of $10^6 - 10^7$ i/c ID_{50}/g may be widely dispersed in the LRS.

Other Tissues

Other tissues may have some infectivity, but at much lower levels than CNS, eye or LRS tissues

2.29 These infectivity estimates have been combined with possible transmission routes to give infectivity estimates for exposed tissues in subsequent patients. These estimates in Table 3 assume that instruments come into contact with similar tissues in the CJD patient and subsequent patients.

Table 3 Potential infectivity in variant CJD, by source tissue and site of exposure

Source tissues and tissues exposed during surgery	Disease stage	Infectivity [ID_{50}/g]
CNS to CNS (or retina or optic nerve)	First 60% of incubation period	$0 - 10^4$
	Last 40% of incubation period and during clinical disease	10^8 (this could increase to 10^9 in the final year and to 10^{10} after the onset of symptoms)
Other parts of eye to other parts of eye	First 60% of incubation period	$0 - 10^4$
	Last 40% of incubation period and during clinical disease	$10^5 - 10^6$
LRS to LRS	All of the incubation period and during clinical disease	$10^5 - 10^6$
Remaining tissues, including blood	All of the incubation period and during clinical disease	$0 - 10^4$

[b] Infectivity is expressed as an ID_{50}. This is the dose that is expected to cause disease in 50% of the recipients to whom it is administered. A pre-script, indicates the route of administration. Thus for a tissue that contains 1 i/c ID_{50}/g, one gram of tissue contains a dose which, when given by intracerebral inoculation, is expected to infect 50% of recipients.

Infectivity of tissues in sporadic CJD

Infectivity in the brain, spinal cord and eye

2.30 PrP^{Sc} has been detected in the brain and spinal cord and eye (personal communication, Professor James Ironside) of patients with sporadic CJD. High levels of infectivity have also been found in the brain and eye tissue of patients who have died of sporadic CJD[24]. **A, C**

2.31 There have been 267 reports of transmission of sporadic CJD by medical procedures throughout the world[25]. These have followed treatment with growth hormone, dura mater grafts, neurosurgery, treatment with gonadotropin, corneal transplants and stereotactic EEG. These data are summarised in Table 4. **B**

Table 4 Global cases of iatrogenic transmission of CJD (up to July 2000)[25]

Mode of infection	Number of patients infected
Tissues/Organs	
Growth Hormone	139
Dura mater graft	114*
Gonadotropin	4
Surgery/invasive procedures	
Neurosurgery	5†
Corneal transplant	3#
Stereotactic EEG	2

*In two cases, dura was used to embolise vessels of non-CNS tissues, rather than as intracranial grafts.
†Contaminated neurosurgical instruments
#One definite, one probable and one possible case.

2.32 The level of PrP^{Sc} in the brain, spinal cord, retina and optic nerve in sporadic CJD is thought to be similar to levels in variant CJD.

2.33 Experiments in which corneas from humans and guinea pigs infected with CJD have been transplanted into animals indicate that corneas can transmit CJD[26 27]. **A, D**

2.34 Transmission of sporadic CJD has been reported after corneal graft operations[28 29]. It is not known whether other parts of the anterior eye are infective. **B**

Infectivity in other tissues

2.35 Most evidence indicates that in sporadic CJD tissues outside the nervous system, including the LRS, do not contain significant levels of infectivity[14] **C.**

2.36 However, one report suggested that low levels of infectivity are present in the kidney, liver and lung tissues of patients with sporadic CJD[24]. This report did not demonstrate infectivity in several other peripheral tissues including peripheral nerve, intestine and blood. **A**

2.37 Interpretation of the positive findings is uncertain, and further work is needed to confirm or refute these observations. This guidance assumes that if any tissues outside the nervous system are infective in sporadic CJD, then it is only with low levels of infectivity.

2.38 A recent experiment on dental tissues from patients with sporadic CJD did not detect PrP^{Sc}, but further work is needed in this area. **C**

2.39 The incubation period for sporadic CJD is not known. For practical purposes, this guidance assumes that the incubation period is 20 years. This assumption is used to estimate the duration of infectivity of tissues such as the brain and eye.

Conclusions on tissue infectivity

2.40 The likely infectivity of tissues from patients with sporadic and variant CJD are summarised in Table 5. These relative infectivity levels are based on current knowledge and advice from SEAC. Dental tissues will be added at a later date.

Table 5 Tissue infectivity in sporadic and variant CJD

Tissue	Sporadic CJD	Variant CJD
Brain, spinal cord, cranial and spinal ganglia, dura mater	High	High
Optic nerve and retina	High	High
Other eye tissues	Medium	Medium
Appendix	Low	Medium
Tonsil	Low	Medium
Spleen	Low	Medium
Other lymphoreticular tissues	Low	Medium
Blood[1]	Low	Low
Other tissues	Low	Low

High: >=10^7 ID_{50}/g[c]; Medium 10^4-10^7 ID_{50}/g; Low <$10^4$$ID_{50}$/g

[1] See section on infectivity in blood.

Infectivity transmitted via instruments

2.41 Instruments may be contaminated with prion agents during contact with infective tissue in surgery. There is concern that prion agents can resist normal decontamination processes, and that infectivity may remain on instruments when they are used on other patients.

2.42 Little evidence is available in this area, which is the subject of a research programme. Until further evidence becomes available, this guidance builds on the assumptions made in the surgical risk assessment1 endorsed by SEAC.

2.43 The amount of infective material contaminating an instrument following surgery depends on the type of instrument and the tissues with which it is contaminated. This guidance follows the assumptions used in the surgical risk assessment[1] that an average of 10 mg of material could remain on an instrument. This is derived from an estimate that 5mg may adhere to an instrument with plane surfaces, such as a blade[31]. This is an area of considerable uncertainty, but the amount of material contaminating an instrument directly after surgery is less important than the amount that remains after decontamination.

c 10^7 is a mathematical expression for 10×10×10×10×10×10×10 = 10,000,000

2.44 A *decontamination cycle* for a surgical instrument involves two stages; physical cleaning, typically using a mechanical washer/drier; followed by inactivation of any remaining infectious material, e.g by autoclaving.

Cleaning

2.45 Instruments undergo a large number of decontamination cycles during their working lives. Studies on instruments with flat surfaces indicate that the first cycle of cleaning may reduce the amount of protein on an instrument by 10^3 [32]. However, instruments with serrated edges and hinges, and others, and others with narrow lumens such as flexible endoscopes, are much more difficult to clean. This guidance follows the assumptions made in the Risk Assessment[1] that cleaning is likely to reduce the infectivity remaining on an instrument by a factor of 10^2 to 10^3.

2.46 Subsequent cleaning rounds are likely to be much less effective as any material that has survived the first cleaning cycle may have been baked on during further processing. There is little experimental evidence on how much would remain. This guidance follows the assumptions made in the surgical risk assessment[1] that subsequent cleaning cycles could reduce the amount of infectivity remaining on an instrument by as much as a factor of 10^2.

2.47 This guidance uses the assumption of the ACDP/SEAC Joint Working Group on TSEs, that cross-contamination of instruments during cleaning was unlikely to occur. This was because in a wet environment, and in the presence of detergents, proteins are unlikely to migrate from one surface and stick on another.

Inactivation

2.48 Inactivation is generally carried out by high pressure steam autoclaving of instruments. Different autoclaving processes vary in their effectiveness in inactivating prion agents[33]. The effectiveness may be altered by small differences in temperature[34]. This guidance uses the assumptions made in the Risk Assessment[1], that the first autoclaving cycle would achieve a 10^3 to 10^6-fold reduction in infectivity. **C**

2.49 Subsequent autoclaving cycles may have less additional effect. This guidance follows the assumptions made in the surgical risk assessment[1] that these could achieve up to 10^3-fold reduction in infectivity.

2.50 It is possible that even following a great many cycles of use and decontamination, some infectivity remains on instruments. This guidance assumes that any infectivity that has resisted removal and remained on instruments, would be firmly attached and unlikely to transfer to subsequent patients during normal surgical procedures. This guidance follows the provisional assumptions made in the surgical risk assessment[1], that infective material must be transferred from an instrument into a subsequent patient for disease transmission to take place.

Combined effect of cleaning and inactivation

2.51 This guidance follows the assumptions made in the surgical risk assessment[1] that the first washing and autoclaving cycles combined would achieve at least a 10^5-fold reduction in infectivity. Subsequent cycles may have much less effect. In ideal conditions decontamination processes are likely to be even more effective but these cautious estimates allow for less than optimal working practices.

2.52 A major research programme into instrument decontamination is underway and the results of these studies may provide some of the basic information that is currently lacking in this area. This guidance will be revised as new evidence becomes available.

2.53 The guidance assumes that infectious and non-infectious material is removed from instruments in similar proportions. There is as yet no data to suggest otherwise.

2.54 The likely effectiveness of instrument decontamination is summarised in Table 6. This summarises the assumptions made in the surgical risk assessment[1] endorsed by SEAC.

Table 6 Effectiveness of instrument decontamination

Variable	Value/range
Initial amount of material on instruments (mean, per instrument)	10 milligrams
Cleaning (washing/disinfecting)	
Reduction in amount of material after first cleaning	$10^2 - 10^3$ fold reduction
Reduction in amount of material after subsequent cleanings	$0 - 10^2$ fold reduction
Deactivation (sterilising/autoclaving)	
Reduction in infectivity after first autoclaving	$10^3 - 10^6$ fold reduction
Reduction in infectivity after subsequent autoclaving	$0 - 10^3$ fold reduction

Type of instruments used

2.55 Decontamination is affected by an instrument's material and construction – whether it has joints, lumens, serrated jaws, ratchets etc. (**Annex 2** categorises types of instrument by their ease of decontamination).

2.56 In some cases, only parts of instruments may come into contact with infective tissues (for example drill bits or the probe in a stereotactic frame). These may cross-contaminate the rest of the instrument.

2.57 Some instruments cannot be autoclaved. These include flexible endoscopes and other optical equipment. Glutaraldehyde is sometimes used to decontaminate rigid endoscopes. However, this is likely to stabilise any proteins present on the instruments.

2.58 Endoscopes are more difficult to decontaminate effectively than normal stainless steel instruments, and this problem is increased if biopsies are carried out using endoscopes. Endoscopes that come into contact with LRS and other infective tissue may continue to pose a risk to subsequent patients despite going through many cycles of use and decontamination. Certain CNS procedures also use devices that are very difficult to decontaminate – e.g. ventricular endoscopes and these may be considered separately.

Modelling scenarios

2.59 Scenarios modelling the infection risk for subsequent patients following surgery on a 'index' patient with CJD are illustrated in Figures 2–5. These scenarios use different tissue infectivity levels in the 'index' patient and different proportions of contaminating prion protein transferred from the instruments to subsequent patients. In each scenario the risk of transmitting infection drops dramatically for subsequent patients and is close to zero before the 10th reuse of an instrument.

2.60 These scenarios have been prepared by the Economics and Operational Research Division of the Department of Health, and are based on the following assumptions:

- 20 instruments are used per operation.
- Each instrument used is initially contaminated with 10 mg of tissue.
- The first decontamination cycle reduces contamination by a factor of 10^5
- Subsequent decontamination cycles reduce contamination by a factor of 10.
- The instruments contact the same type of tissue in the CJD and subsequent patients.

Figure 2 Scenario modelling probability of infecting subsequent patients. Tissue Infectivity 10^{10} ID_{50}/g (e.g. CNS in patient with symptoms of CJD)

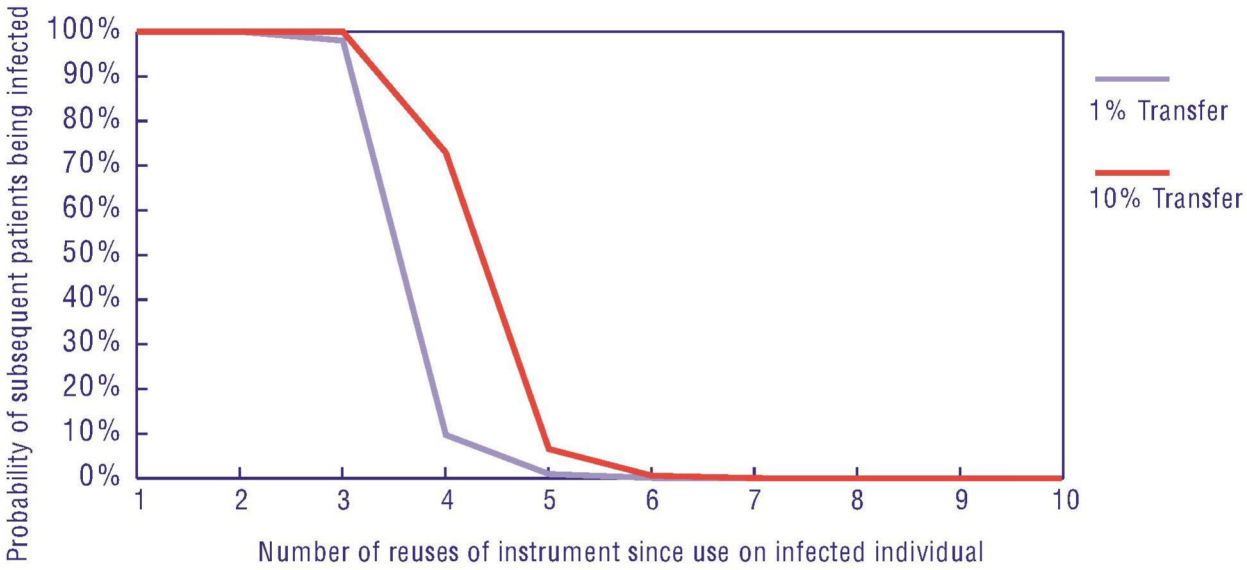


Figure 3 Scenario modelling probability of infecting subsequent patients. Tissue Infectivity 10^{8} ID_{50}/g (e.g. CNS in patient in the later stages of incubation period)

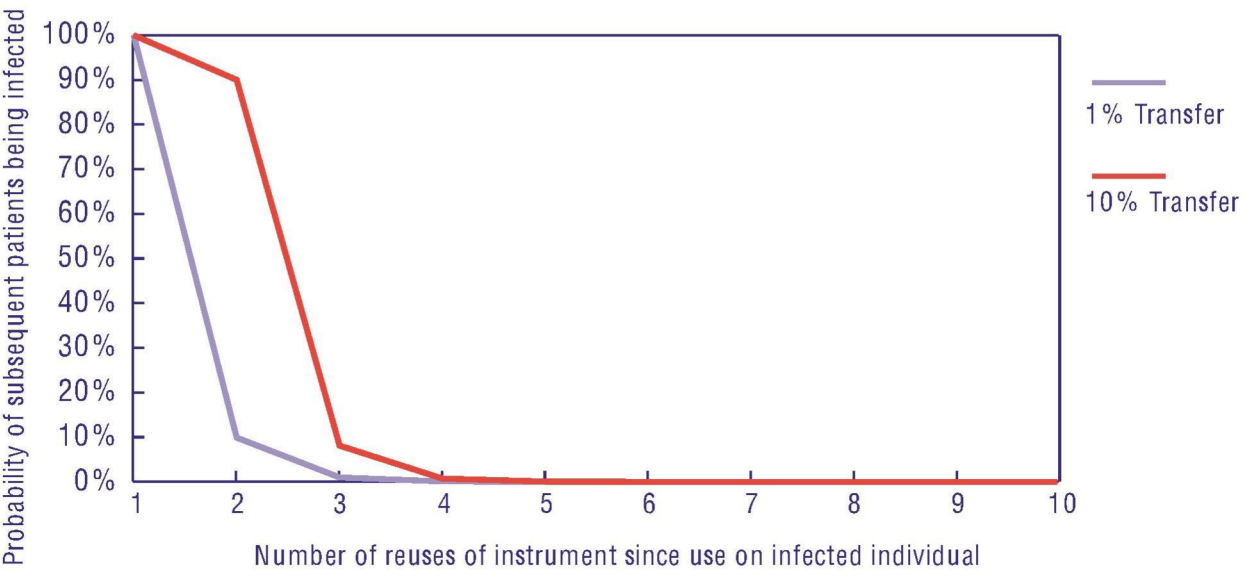


Figure 4 Scenario modelling probability of infecting subsequent patients. Tissue Infectivity 10^6 ID_{50}/g (LRS or anterior eye in patient at any stage of CJD infection, more pessimistic assumption)

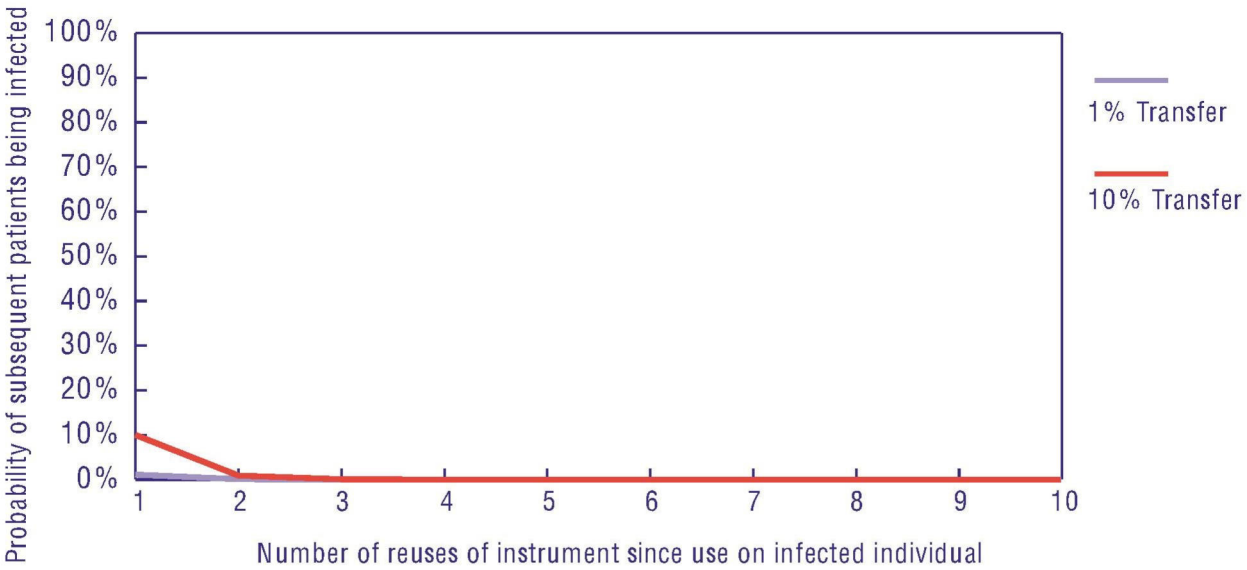
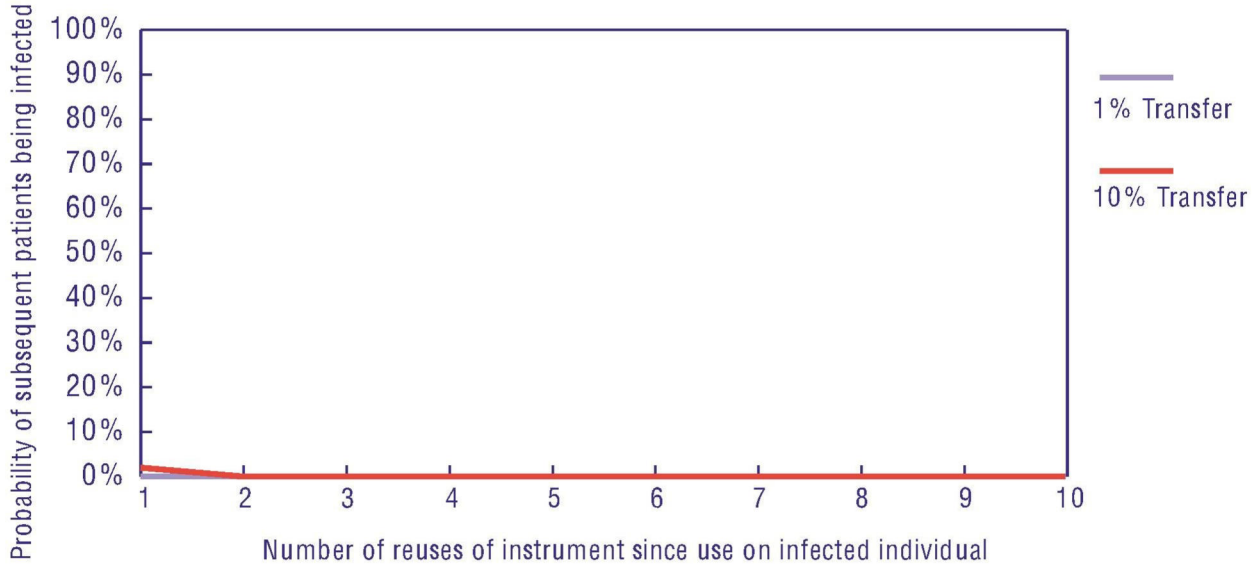


Figure 5 Scenario modelling probability of infecting subsequent patients. Tissue Infectivity 10^5 ID_{50}/g (LRS or anterior eye of patient in any stage of CJD infection, less pessimistic assumption)



Conclusions

2.61 On the basis of the preceding evidence and reasoning, most instruments that have gone through ten cycles of use and decontamination are unlikely to pose a significant risk. However, this is an area of active research, and the CJD Incidents Panel should consider the type of instrument used in each incident as some are particularly difficult to decontaminate.

Infectivity of Blood Components and Plasma derivatives

Definitions

2.62 This section deals with the potential infectivity of blood components and plasma derivatives produced from blood donated from people who go on to develop CJD.

2.63 Blood components are derived from a single blood or plasma donation or in the case of platelets, a small pool usually of about four donations. These are labile products with a short shelf life. Blood components include whole blood, red cell concentrates; platelets (cell fragments involved in blood clotting), granulocytes (a form of white blood cell), fresh frozen plasma, and cryoprecipitate (made by freezing and thawing plasma).

2.64 Plasma derivatives are prepared from human plasma pooled from a large number of donations. These products have a long shelf life and, unlike blood components, are licensed medicinal products. Plasma derivatives include clotting factors, immunoglobulins, albumin, and anti-thrombin.

Background

2.65 This document builds on the information summarised in the blood risk assessment[2], which has been accepted by SEAC. This risk assessment will be reviewed to reflect new research on plasma derivatives and the effects of purification processes. This section will be revised when the new assessment becomes available.

2.66 There is no epidemiological evidence that any form of CJD (familial, sporadic or variant CJD) has ever been transmitted as a result of treatment with blood components or plasma derivatives. Studies of recipients of blood donated by people who go on to develop sporadic CJD, and studies of sporadic CJD prevalence among haemophiliacs, have not demonstrated an increased risk of developing CJD[2,35]. **B**

Variant CJD

2.67 In variant CJD the disease process involves many tissues, including the LRS. There is however, no evidence that variant CJD can be transmitted by blood components or plasma derivatives. However, variant CJD is a new disease with a long incubation period, and it may be too soon for cases transmitted by this route to be detected.

2.68 Evidence on the possible infectivity of blood in variant CJD is limited. One study has investigated whether blood from people with variant CJD can transmit the disease to mice[5]. This study did not detect infectivity in plasma or in buffy coat (a blood fraction rich in white cells and platelets). However, the methods used had a detection limit of about 200 human i/v ID_{50}s per ml, and therefore would not have detected levels of infectivity that could result in transmission of variant CJD in humans. **A**

2.69 Even low infectivity levels could be important because large quantities of blood and plasma derivatives are used to treat individual patients. These quantities greatly exceed the trace amount of protein remaining on surgical instruments after decontamination.

2.70 Another research study failed to detect any PrP^{Sc} in the buffy coat of blood of a patient with variant CJD[9]. The detection limits of the techniques used meant that if any PrP^{Sc} was present, it must have been at a concentration 300,000-fold lower than that found in the patient's brain. **C**

2.71 Research is also being carried out on whether BSE can be transmitted between sheep by whole blood transfusion[36]. BSE has been transmitted to one transfused animal. This study is ongoing, and it is not yet possible to estimate the infectivity levels. **D**

Whole blood

2.72 The infectivity of whole blood is estimated as most likely to be 1 i/v ID_{50} per ml. This estimate is drawn from the blood risk assessment, and is based on infectivity levels reported in the blood of hamsters infected with scrapie, and in mice infected with a familial form of human CJD. The relevance of this model to estimates of infectivity in the blood of variant CJD in humans is uncertain. However, the data from studies of people with variant CJD are consistent with infectivity values ranging from zero to 200 i/v ID_{50}s per ml[5].

2.73 Infectivity in blood is assumed to be constant throughout the incubation period for variant CJD. For practical purposes, the earliest time that patients could start to incubate the disease is taken to be the onset of the BSE epidemic in 1980.

2.74 The route of administration affects the transmission of TSEs in animal models. The intravenous and intramuscular routes used for blood components and plasma derivatives are less efficient than direct inoculation into the brain. This document follows the assumption made in the blood risk assessment[2] report, that the intravenous route is 10 times less efficient than the intra-cerebral route. Recent studies by Brown *et al* suggest a comparable value[37].

Leucodepletion

2.75 The LRS is involved in variant CJD and this raises the possibility that white blood cells could contain infectivity. While this has not been demonstrated, leucodepletion (removal of white blood cells) has been carried out on all UK-sourced blood since 1999 as a precautionary measure. In the absence of convincing evidence, this guidance has not made any assumptions about the effect of leucodepletion on infectivity.

Blood components

2.76 Most modern treatments use blood components rather than whole blood. The literature on infectivity of different components of blood was reviewed as part of the blood risk assessment. This concluded that studies carried out on familial CJD in mice provide the best available model for the distribution of infectivity in variant CJD in human blood[38]. However, this model may not be directly relevant to infectivity in the blood of humans with variant CJD. One recent study has reported experimental transmission of BSE in a sheep model following experimental infection. It may be that data emerging from this model will be more relevant to variant CJD in humans. **D**

2.77 Other studies have examined infectivity in blood that has been 'spiked' with brain material from hamsters infected with scrapie. This model has also been used to investigate the effects of different processing steps on infectivity. However, these experiments may not give a true impression of the distribution of infectivity in blood in people with variant CJD. This guidance and the blood risk assessment have only drawn on data from these experiments when no other information is available.

2.78 Estimates for infectivity used in the blood risk assessment are reproduced in Table 7.

2.79 These results should be interpreted with some caution as the distribution of infectivity within blood in people with variant CJD may well differ from that found in mice infected with a familial human prion disease. Also, the fractionating procedures used in the mice experiments may not be directly comparable with those used for human blood.

Table 7 Possible infectivity levels of blood components in variant CJD

Component	Infectivity per ml (iv ID_{50}/ml)	Infectivity per unit (iv ID_{50}/unit)
whole blood	1	450
plasma	1	200
White cells + platelets	7	100
red cells	0.005-1*	1-200*
cryo-precipitate	8	20

*This depends on the purification processes used

2.80 Preparations of red cells and plasma with varying degrees of purity are transfused into patients. Given the uncertainties over the infectivity values in general, and over how infectivity is distributed between white cells and platelets, this guidance assumes that the infectivity of platelet preparations is the same as the mixed white cell plus platelets fraction.

2.81 The figures in Table 7 are based on very uncertain estimates from the blood risk assessment[2] that are derived from the data from Brown *et al* 1998[38]. However studies using the same model that have been published since the blood risk assessment[37 39] give similar estimates for infectivity.

2.82 Patients usually receive more than one unit in a transfusion, and may be transfused several times. Even so a patient is unlikely to receive more than one unit of a blood component from a particular donor with variant CJD.

Estimates of infectivity in plasma derivatives

2.83 Plasma is estimated to have approximately the same infectivity as whole blood, i.e. 1 ID_{50}/ml (see Table 7). The infectivity in plasma derivatives depends on the size of the pool of donations used to manufacture the derivative, the effect of processing, and the amount administered.

Size of donor pool

2.84 Tens of thousands of donations of plasma may be combined to prepare plasma derivatives, so greatly diluting any single infected donation. For example, if plasma derivatives are derived from a pool of 20,000 donations, then the infectivity in the starting product is estimated to be 0.5×10^{-4} iv ID_{50}/ml.

2.85 Specific immunoglobulins (e.g. anti-D, hepatitis B, tetanus, rabies, Varicella zoster) are produced from much smaller pools of donations. The number of donations used depends on the type of immunoglobulin and the producer, and ranges from less than 50 to 4,000.

2.86 In specific incidents, the size of the pool used should be used to calculate the potential infectivity of plasma derivatives.

Effect of processing

2.87 Plasma derivatives undergo various processing stages including cryoprecipitation, extraction with ethanol, precipitation, filtration, partitioning, virus inactivation and heat treatment.

2.88 Discussions on the effect the different processing steps for various products have been based on the known characteristics of infectivity isolated from brain. Studies on the effects of processing on infectivity have also been carried out on hamster blood 'spiked' with brain material infected with scrapie. However the characteristics of any infectivity that might be present in blood could be quite different from that found in the brain.

Dose

2.89 A 'dose' of a plasma derivative may contain high concentrations of proteins. Some clinical conditions require repeated doses, so that large amounts may be given over a period of time. This is important as patients could receive multiple doses from the same possibly contaminated batch of plasma derivative. This document assumes that the risks from such repeated doses of variant CJD would be additive.

Infectivity

2.90 The risk from plasma derivatives is even more uncertain than from blood components. Further risk assessment work is being carried out on the infectivity of different fractions and the effects of processing. In the meantime, this guidance provides an interim assessment of the risk, based on the blood risk assessment.

2.91 The blood risk assessment based its infectivity calculations on a combination of the low dose and spiking experiments of Brown et al 1998. It assumed that the infectivity (per gram of protein) in the end-product plasma derivatives was the same as in the plasma fraction from which it was derived. The calculations ignore any possible dilution effects arising from the pooling of plasma donations. The infectivity values in Table 8 are derived from the blood risk assessment.

Table 8 Estimates of the infectivity of plasma derivatives in variant CJD

Derivative	Infectivity[a]
Factor 8 (Crude)	24 ID_{50} per standard dose of 2000 iu
Factor 8 (Highly purified)	4 * 10^{-2} ID_{50} per standard dose of 2000 iu
Factor 9	4 * 10^{-1} ID_{50} per standard dose of 1250 iu
Normal Immunoglobulin	660 ID_{50} per 90g intravenous dose
Albumin 20%	2 * 10^{-3} ID_{50} per standard dose of 100ml

a These values ignore any possible dilution effect arising from the pooling of plasma donations.

2.92 The blood risk assessment did not provide estimates of infectivity values for any other plasma derivatives.

Conclusions

2.93 While the pool size and processing details will need to be assessed for each incident, it seems clear that albumin, Factor IX, and high purity Factor VIII are all likely to have low infectivity levels.

2.94 Crude factor VIII and immunoglobulin may, however, be of concern. The management of incidents involving these, and other plasma derivatives is discussed in section 6.

2.95 These risks will be reassessed once a revised estimate of infectivity has been completed.

Sporadic CJD

2.96 There is no epidemiological evidence that sporadic CJD has ever been transmitted as a result of treatment with blood components or plasma derivatives[2]. **B**

2.97 There is a general consensus that blood components and fractionated plasma derivatives prepared from donors who go on to develop sporadic CJD, are unlikely to increase the risk of recipients developing the disease. This guidance has not attempted to further characterise this risk.

Susceptibility of subsequent patients

2.98 All patients with variant CJD for whom genetic information is available have the same genotype (methionine homozygous) at codon 129 position on the PrP gene. This does not mean that other genotypes are not susceptible. Indeed, patients with other genotypes have been infected with CJD following treatment with contaminated growth hormone[40].

Conclusions

2.99 The role of genetic susceptibility in the transmission of CJD between people is unclear. Until the role of genetics is better understood, it is prudent to assume that everyone is equally susceptible to transmission from CJD, although the incubation period may vary.

Summary of infectivity of blood components and surgical instruments

2.100 The risks from blood components and plasma derivatives are unknown. However, should blood be infective, the risk from blood components could be on a par with that from surgical instruments. This is because the quantity of a blood component used to treat patients is much larger than the traces of tissue transferred to patients from contaminated surgical instruments. This means that even relatively low infectivity levels may be of concern. Table 9 compares the possible infectivity transmitted to patients following surgery with that following treatment with blood components (variant CJD only).

Table 9 Comparison of possible infectivity of blood components and surgical instruments

Source tissues and tissues exposed during surgery (all CJD)	Possible infectivity transferred to next patient per procedure[2]
CNS to CNS, or optic nerve/retina to optic nerve/retina (last 40% of incubation period)	20 ID_{50}
Other eye tissues to other eye tissues (last 40% of incubation period) or LRS to LRS for whole duration of infection	0.2 ID_{50}
Blood components (Variant CJD Only) – whole duration of infection	**Possible infectivity per unit**
whole blood, plasma, white cells + platelets, red cells, cryoprecipitate	Possibly zero, but estimates for different components range from 20-450 ID_{50}[1]

1 See Table 7

2 Assuming an infectivity of 10^8 ID_{50}/g for CNS and back of the eye to similar tissues; an infectivity of 10^6 ID_{50}/g for other eye tissues and LRS to similar tissues; 10 mg initial load per instrument; 20 instruments per procedure; 10^5-fold decrease in infectivity by decontamination and a 10% transfer of residual infectivity to the subsequent patient.

Clinical procedures categorisation by risk

2.101 This document categorises clinical procedures according to their likely risk of transmission of prion proteins. In sporadic CJD, only CNS and the eye pose a major risk. These categories are summarised in Table 10. **Annex 3** provides a detailed breakdown by type of operations.

Table 10 Clinical procedures – categorisation by possible risk[a]

High risk procedures
All procedures that involve piercing the dura, or contact with cranial ganglia (including the trigeminal and dorsal root ganglia), or the pineal and pituitary glands.
Procedures involving the optic nerve and retina.
Treatment with blood components. **Variant CJD only**
Medium risk procedures
Other procedures involving the eye, including the conjunctiva, cornea, sclera and iris.
Procedures involving contact with lymphoreticular system (LRS). **Variant CJD only**
Anaesthetic procedures that involve contact with LRS during tonsil surgery (for example laryngeal masks). **Variant CJD only**
In certain instances only, to be assessed for each batch of product, treatment with high doses of specific immunoglobulins, normal immunoglobulin and certain clotting factors. **Variant CJD only**
Low risk procedures
All other invasive procedures including other anaesthetic procedures.
Treatment with albumin, Factor IX, and high purity Factor VIII and certain doses of normal immunoglobulins. **Variant CJD**
Treatment with any blood component or product. **Sporadic CJD**

a Applies to both sporadic and variant CJD unless otherwise stated

Section 3: Public Health Investigation of Incidents

3.1 This section describes the role of the local health teams and the Department of Health's CJD Incidents Panel in investigating incidents that involve invasive medical procedures. The investigation of incidents involving blood donations is covered in Section 5. Advice on the investigation of incidents involving tissue and organ donation will be added at a later date.

3.2 Health Authorities are currently responsible for protecting the population from communicable disease. The public health response to an incident involving possible exposure to CJD through an invasive medical procedure will usually be led by the Consultant in Communicable Disease Control (CCDC).

3.3 In all incidents, the CCDC should contact the Department of Health secretariat to the CJD Incidents Panel.

Identifying possible exposures to CJD in healthcare settings

3.4 The National CJD Surveillance Unit (CJDSU) collects, manages and analyses information on all suspect cases of CJD in the UK. Suspect cases are referred to the CJDSU by clinicians. A neurologist from the unit then visits each case and assigns them to a diagnostic category.

3.5 The clinician caring for the patient should inform the Consultant in Communicable Disease Control (CCDC), or equivalent, about all possible, probable and confirmed cases of sporadic and variant CJD. This reporting system is described in recent guidance prepared by the CJDSU, the Public Health Medicine Environmental Group and the UK Health Departments .

3.6 The CCDC is responsible for co-ordinating the initial response to this information including contacting the Department of Health's CJD Incidents Panel.

3.7 Should other local professionals become aware of a possible incident, they should contact the local CCDC who will liase with the CJDSU and the Incidents Panel.

Initial Information Collection

3.8 The CCDC should gather the initial information on the case so that the Incidents Panel can assess the need for immediate action. The CCDC should use the reporting form in **Annex 4** to collect information on the clinical status of the patient with CJD, and the invasive medical procedures carried out on this patient.

3.9 The CCDC or their equivalents from all parts of the UK should swiftly inform the Department of Health secretariat to the CJD Incidents Panel about incidents. Those from Scotland, Wales and Northern Ireland should also send a copy of the notification to the medical officer in their respective Health Department with responsibility for CJD.

3.10 The contact point for the Incidents Panel is Dr Philippa Edwards at the Department of Health.

Telephone: GRO-C Fax: GRO-C

E-mail: philippa.edwards@ GRO-C

Initial Appraisal and Control Measures

3.11 The CJD Incidents Panel will rapidly appraise the information on the reporting form, and decide:

either

that there is no significant risk to other patients and no further action is required.

or

that there may be a risk to other patients and that the potentially contaminated instruments should be removed from use (quarantined). This should be carried out following the ACDP/SEAC Guidance[3]. The CJD Incidents Panel will advise on what additional information is required to assess the risk to other patients.

Further information to characterise risk

3.12 Where further investigation is required, the CCDC may set up a local incident management team. Epidemiologists from the PHLS Communicable Disease Surveillance Centre (CDSC) may assist with any risk characterisation exercise, particularly when more than one health authority is involved. This arrangement pertains to Scotland, Wales and Northern Ireland.

3.13 The team should collect detailed information about the surgical instruments used on the patient with CJD and the patients who may have been exposed to each instrument (Table 11). This information should be presented to the Incidents Panel so that the potential risks may be assessed and managed.

Table 11 Further information required to characterise risk

Surgical instruments
Description of instruments including name, make, size, function and any identifying number.
Standards of documentation of use and decontamination of instruments.
Details of subsequent use of the instruments.
Number of times the instruments have been reused.
Details of decontamination procedures.
Date of removal if the instruments have been removed from clinical use.
Information on whether the instruments have remained in the same set.
If use and decontamination of instruments are not documented, information will also be required on:
Number of instruments in use at the time of the index patient's procedure.
Number of procedures for which they are used prior to being discarded.
Number and type of procedures for which these instruments are used in a given time period.
Possibly exposed patients
Number of patients definitely and possibly exposed to the instruments.
Details of how they are identified as being definitely or possibly exposed.
Date, location and type of procedures in which instruments were definitely or possibly used.
Tissues to which the instruments would have been exposed during these procedures.

Risk assessment

3.14 The Incidents Panel will assess the risk of exposure to CJD to subsequent patients by reviewing the data collected by the local incident team. In each case the Panel will consider the clinical condition of the patient, the type of instruments used, the decontamination processes in place and whether the instruments can be traced.

Question Box: Investigation of incidents

We have proposed a system to identify and investigate incidents involving surgical procedures carried out on people who later develop CJD. This would build on existing public health systems, both locally and nationally.

Q1 Do you agree with our proposals for investigating and managing surgical incidents?

Section 4: Public Health Management of Surgical Incidents

4.1 While the risk of transmitting CJD through invasive medical procedures is uncertain, precautionary action should be taken to prevent the possible transmission of infection. It is also important to collect information about possible exposures to CJD so that the risk of transmitting CJD can be better understood. It is important to ensure that actions taken to protect the public health do not prejudice individual patient care.

4.2 The Incidents Panel will advise the local Incident Management Team on the action required to manage incidents involving possible exposure to CJD in healthcare settings. These actions have four main aims:

- To prevent transmission of CJD from potentially contaminated instruments.
- To prevent further transmission of CJD through healthcare from exposed patients who are considered to have a significant risk of having contracted CJD.
- To collect information on people who could have been exposed to further our understanding of the risk of transmitting CJD in healthcare settings.
- To inform the public about a local incident.

4.3 The Incidents Panel will use the algorithm in **Annex 5** to help make decisions on managing possibly exposed patients and instruments. The decision points in the algorithm are not automatic, and multiple factors will need to be considered for each case.

Instruments

4.4 In most circumstances, instruments used on the 'index patient' will already have been re-used many times by the time the patient is diagnosed. It follows that most of the risk associated with these instruments will have already occurred.

4.5 Nevertheless, there are grounds for a strongly precautionary approach toward instruments, withdrawing all those that *might* be implicated as soon as possible. Where it is necessary to destroy instruments, this should be done by incineration where possible, as described in the ACDP/SEAC Guidance[3].

4.6 In general, instruments that have undergone **ten or fewer decontamination cycles** since being used on the index patient with CJD should be incinerated. Some of these instruments are of potential research value and the Panel will advise on this.

4.7 The Panel may advise that particular instruments are incinerated even if they have undergone more than 10 decontamination cycles. This may be because they are difficult to clean, or because they can not be mechanically washed or autoclaved.

4.8 This advice should not be interpreted as meaning that possibly contaminated instruments may be repeatedly decontaminated and then returned to use. This is because current scientific knowledge is insufficient to be sure that such instruments would be safe.

4.9 If instrument tracing systems are inadequate, it may not be possible to identify the instruments used on the index patient with CJD. In these cases, **any** instrument that may have been used on the index patient, and is not known to have undergone at least 10 decontamination cycles might have to be incinerated.

Question Box: The surgical instruments

Q2 Do you agree with our proposal that instruments used on infective tissues of patients who later develop CJD, may continue to be used if they are judged to have undergone a sufficient number of cycles of use and decontamination?

Q3. Do you agree with our proposal that instruments that have not undergone a sufficient number of cycles of use and decontamination, should be permanently removed from use (either destroyed or used for research)?

People with a 'contactable risk' of CJD

4.10 While the risk of transmitting CJD through invasive medical procedures is very uncertain, the modelling set out in figures 2–5 in Section 2 shows that some patients are likely to be at a higher risk than others. The modelling indicates that patients who have undergone procedures with instruments that have only undergone a small number of cycles of use and decontamination since being used on tissues infective for CJD, will be at a greater risk of becoming infected than other exposed patients.

4.11 If these patients do acquire CJD, then they too could pose a risk to others. Therefore these people should be contacted and informed about their possible risk. This is in order to protect public health by advising these individuals not to donate blood, organs or tissues. They should also be advised to inform their carers should they require further surgery. Details of patients in this group should also be recorded on the confidential database (see paragraphs 4.19–4.25). These individuals would not have the option of removing their details from this database

4.12 The CJD Incidents Panel will advise the Incident Management Team on how many people should be included in this 'contactable' group [**Annex 5**]. The size of this group will depend on the infectivity of the source tissues in the 'index' patient with CJD [Table 8].

4.13 If instrument tracing systems are inadequate, it may not be possible to identify these patients with certainty. Decisions on the group to be contacted should then be made by the CJD Incidents Panel on a case-by-case basis.

Table 12 Patients to be included in 'contractable' group

Clinical procedure in index patient[d]	'Contactable' group
High risk procedures	
CNS, retina, optic nerve procedures in patient with symptoms or within one year of developing symptoms of any type of CJD	First 6 patients
CNS, retina, optic nerve procedures in patient who subsequently develop any type of CJD (in last 40% of incubation period*).	First 4 patients
Medium risk procedures	
Other eye tissue procedures in patients who have, or subsequently develop any type of CJD (in last 40% of incubation period*).	First 2 patients
LRS procedures in patients who have, or subsequently develop variant CJD (at any stage in incubation period).	First 2 patients

* In sporadic CJD the mean incubation period is assumed to be 20 years. In variant CJD the incubation period is assumed to start in 1980.

4.14 The CCDC should inform the patients' general practitioners and the UK Blood Service.

4.15 Particularly sensitive arrangements will be needed for informing patients that they are included in this group. This information will be burdensome and of little overall benefit to the individuals themselves. It might additionally result in practical difficulties (e.g. insurance).

4.16 We would hope that the task of informing patients would be readily accepted by an appropriate clinician already responsible for the individual's care, in many cases their general practitioner. However a small cadre of individuals should be developed, knowledgeable as to the broader aspects of CJD and experienced in discussing its implications, from whom those clinicians could expect active support up to and including sharing the relevant consultation(s).

4.17 Appointments should be scheduled at such a time and be of sufficient length to allow exploration of issues and concerns. There should be a facility to supplement advice with telephone contact and a further appointment if required. Written material supporting the consultation, to be taken away, will be available, prepared under the auspices of the CJD Incidents Panel.

4.18 In essence, patients will be counselled as to the current incomplete understanding of risk, and requested to collaborate with active follow up by informing whoever manages the database of any changes of address. They will, as stated, be advised against blood or organ donation. They will also be advised of the need to inform their carers if they require further surgery.

Question Box: The 'contactable' group

We propose that public health action may be required for certain patients who have been exposed to CJD. These exposed people should be advised not to donate blood, or organs and to inform their doctors if they require future surgery. We propose that they should be told about their exposure by their doctor, and given appropriate counselling and support.

Q4. Do you agree with our proposals to reduce the risk of further spread of CJD via surgery and donated blood and organs?

Q5 Do you agree with our proposals to contact these exposed patients so that public health actions may be taken to protect others?

d See Box 2 for detailed categorisation of clinical procedures

People with a 'possible' risk of acquiring CJD

4.19 It is unlikely that anyone outside the 'contactable' group would acquire CJD from an incident. Even so Incident Management Teams should collect information on other 'possibly exposed' people so that the risk of transmitting CJD through invasive medical procedures can be better understood.

4.20 To this end, a public health database will be maintained at CDSC. This database will include relevant details of exposed individuals from all countries within the UK. The databse will enable the long term follow up of people possibly exposed in incidents. The database may also be used to contact people should a prophylaxis for sporadic or variant CJD be developed.

4.21 The CJD Incidents Panel will advise the local team which people should be recorded on this confidential public health database.

4.22 It is important that members of the public are aware of the existence of this database, and realise that they are able to a) find out if they are on the database and b) ask for their records to be altered if incorrect, or deleted (see Public Awareness section).

4.23 All patients in the 'contactable' group should be included in this database.

4.24 In general, the Panel will advise that **the first ten patients** operated on with the instruments used on the index patient with CJD should be entered on this database.

4.25 If instrument tracing systems are inadequate, it may not be possible to identify these patients. In this case, anyone who could be one of the first 10 patients should be entered on the database.

Question Box: The 'possibly exposed' group

We propose that a database is set up to enable follow up of all patients who might have been exposed to CJD through medical procedures. While we believe that the risk for most people in this group is low, the database will be used to find out whether any of them develop CJD. This will increase our knowledge and understanding about risks from medical procedures.

We propose that patients (except for those in the contactable group) are not told about their possible exposures and that their details are recorded on the database. We propose that the database is publicised so that individuals are aware of its existence, and can find out about their exposure details and have their names removed from the database if they wish.

Q6. Do you agree with our proposals not to inform possibly exposed people (except for those in the contactable group) of their possible exposure?

Q7. Do you agree with our proposals to set up a database to follow up all possibly exposed people, with the aim of increasing our knowledge of the risk of transmitting CJD through medical interventions?

Q8 Do you agree with our proposal that informed consent should not be sought from individuals before recording their details on the database?

Q9 Do you agree with our proposal that the database should be publicised so that individuals can find out whether they are on it, and about their possible exposures?

Q10 Do you agree with our proposal that individuals (except for those in the contactable group) should be able to remove their names from the database, without having to find out whether they have been put at risk?

Section 5: Interim advice on the investigation and management of incidents involving blood (variant CJD only)

Investigation

5.1 The UK Blood Services (UKBS) work with the CJD Surveillance Unit to identify blood donations from people who later are found to have developed variant CJD[42].

5.2 If blood from donors who later develop variant CJD has been used to produce plasma derivatives, UKBS inform the relevant manufacturer; Bio Products Laboratory for England and Wales, and the Protein Fractionation Centre for Scotland and Northern Ireland.

5.3 The manufacturer can then identify and trace the implicated products. If the products are still within their shelf life, the manufacturer is obliged to notify the incident to the Medicines Control Agency (MCA). The MCA will then advise the manufacturer to recall any implicated products by contacting pharmacy departments, haemophilia centres etc. Where necessary, the MCA facilitates this process by issuing a 'Drug Alert' to health professionals.

5.4 If the products are still within their shelf life the manufacturer is also obliged to inform other companies who have purchased implicated products as ingredients in other medicines.

5.5 If implicated products have been sold overseas, the manufacturer should inform their customers and the regulatory authorities. The MCA will issue a rapid alert to regulatory authorities in other EC member states, and will contact other countries via the WHO.

5.6 If the products are time expired (as is likely to be the case in a variant CJD Incident), recall is not an option, and the manufacturer is not obliged to take any action.

Proposals

5.7 When the UKBS become aware of implicated blood donations, they should inform the local CCDC for the trust(s) where the blood components were used. The CCDC should inform the CJD Incidents Panel about the incident. The CCDC should also inform CDSC who will provide assistance, and help co-ordinate incidents that involve more than one health authority.

5.8 The CCDC, together with the hospital infection control doctor, should then investigate the incident, identifying the recipients of the blood components.

5.9 The UKBS should inform the CJD Incidents Panel if any implicated blood has been used to manufacture plasma derivatives.

5.10 The UKBS should ask the manufacturers to provide the CJD Incidents Panel with the information required to assess the risks from the plasma derivatives. This should include details of the products issued, their manufacture and the number of plasma donations pooled.

Management

Removal of blood from use

5.11 The UKBS are responsible for ensuring that any implicated blood components that are in date are withdrawn from use.

5.12 The relevant manufacturer is responsible for ensuring that implicated plasma derivatives are withdrawn from use.

Blood Components

5.13 While blood has not yet been found to be infective in variant CJD, as a precautionary step, recipients of blood components (red cells, platelets, plasma, white cells, cryoprecipitate) donated by someone who goes on to develop variant CJD should be included in the contactable group.

5.14 The CCDC should ensure that these individuals are informed about their exposure, and receive public health advice. This may be carried out by the patients' GP or other suitable health professional (see Section 4).

5.15 The CCDC should also pass information about these individuals to the CJD Incident database at CDSC.

Plasma Derivatives

5.16 The risk from plasma derivatives is less clear and the CJD Incidents Panel will need to assess each case individually, using the information supplied by the manufacturer.

5.17 As an interim measure (see Section 2), the CJD Incidents Panel may advise contacting recipients of some implicated plasma products where assessment indicates a medium level of risk. In this interim period, advice on the precautions required should these patients undergo surgery may be less stringent than those recommended for the contactable group in surgical incidents.

5.18 As an interim measure the CJD Incidents Panel may advise that recipients of albumin, Factor IX, and high purity Factor VIII need not be contacted, but where possible, they should be recorded on the CJD incidents database.

5.19 The CJD Incidents Panel will ask the manufacturers to inform organisations in their distribution chain, including pharmacy departments and haemophilia centres, about the implicated product.

5.20 The CJD Incidents Panel will provide information to the manufacturer for distribution to these organisations. This will explain which doses of products are unlikely to pose a risk to recipients, and will direct the organisation to contact the local CCDC(s).

5.21 The CCDC will then work with the hospitals and other organisations to identify recipients and collect details of the doses of derivatives that have been given. The CCDC will then pass this data on to CDSC for entry onto the database.

5.22 It may not be possible to identify all recipients. For example, albumin is used in a wide variety of medicinal products, and there may be no way of identifying who has received products made from an implicated batch.

5.23 When the Panel advises that recipients should be contacted, the CCDC should ensure that these individuals are informed about their status, and that public health advice is given. This may be carried out by the patients' GP or other suitable health professional (see Section 4).

Question Box: People who receive implicated blood components and plasma derivatives

Q12. Do you agree with our proposal to include people who have received blood components donated by people who later develop CJD, in the contactable group?

Q13 Do you agree with our proposals to manage people who have received plasma products derived from blood donated by people who later develop CJD?

Section 6: Public awareness

Principles

6.1 Principles of public openness underlie this guidance:-

6.2 Information about CJD should be widely available. This should include information on the current knowledge of the risk of contracting CJD through medical procedures and the actions being taken to improve our knowledge and minimise these risks.

6.3 Members of the public have a right to know about specific incidents and if they could have been exposed to a potential risk. Concerned individuals who wish to find out about possible exposure should be advised that there is currently no test to find out whether someone is incubating CJD and no cure for the disease.

6.4 Health teams should try to avoid informing people about possible risk-exposure against their will. The only exception to this is where there is a need to take action to protect the public health. In these cases patients would always be informed.

6.5 A database of possibly exposed patients will be set up to help to determine the risk of transmitting CJD through invasive medical procedures. Patients have a right to decide whether their personal information is kept on this database. Systems should be set up to allow patients to exercise this right without necessarily having to find out about their own exposure status.

Objectives

6.6 Following on from this, the public communication has five main objectives:-

- To provide general information on CJD, the current knowledge of the risk of contracting CJD through medical procedures and actions being taken to improve our knowledge and minimise these risks.
- To provide general information about particular incidents.
- To provide an opportunity for individuals to discuss, clarify and obtain reassurance about any of this.
- To provide a mechanism for individuals who remain concerned to find out if they were possibly exposed and to receive appropriate local care and support.
- To provide information to concerned individuals about the current lack of a diagnostic test and cure for CJD.
- To provide a mechanism for individuals to remove themselves from the database of exposed individuals without needing to find out if they were actually exposed.

National Information

6.7 The public should have access to information about CJD, what is known about the risk of transmitting CJD through invasive medical procedures, how we are reacting to this situation, and the need for further research.

6.8 The public may be informed through publicity material including leaflets and posters that are made widely available in healthcare settings. A media campaign would also be effective in informing members of the public.

6.9 Additional information should be available on recognised health websites.

6.10 Further information and support may be provided by **NHS Direct**. Equivalent arrangements for Scotland have yet to be established. Until such time information on local incidents should be the subject of local arrangement following the principles described in this document.

Local information in an incident

6.11 The public should have access to information on particular incidents. This should:

- Reiterate the general information outlined above.
- Provide specific information about the incident.
- Provide reassurance where possible.
- Explain the purpose, value and mechanism of the database of exposed people.
- Advertise a means for individuals who remain especially concerned to discuss or clarify any issues.
- Enable individuals who still remain especially concerned to be removed from the database and/or to find out whether they were exposed.

6.12 This would be done in the following ways:

- A press release which refers to the general information leaflet and websites as sources of information (points a to d above).
- These information sources also advertise that individuals who remain concerned can ring **NHS Direct** to discuss the issues involved.

Information for Concerned Individuals

6.13 Individuals who ring NHS Direct speak initially to a Health Information Adviser who notes the caller's demographic details and that this call is related to clinical exposure to CJD. There are then two possible options.

6.14 The concerns are addressed by this Health Information adviser using the attached flowchart **(Annex 6)** and question and answer sheets.

6.15 The call is passed to one of a smaller group of Health Information Advisers who are experienced in this field. They would also use the flow chart and question and answer sheets to address the caller's concerns.

Question Box 2: Public awareness

Q14. Do you agree with our proposals for a national publicity campaign to raise public knowledge and awareness about these risks?

Q15. Do you agree with our proposals for local publicity campaigns for each incident?

Q16. Do you agree with our proposals for enabling concerned individuals to find out about their possible exposures and whether they are on the database?

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Annex 1: Advice and policy on reducing the risk of CJD though medical procedures

Rigorous implementation of washing, decontamination and general hygiene procedures is key in minimising the risk of transmitting CJD on surgical instruments. This is the advice from SEAC which has been incorporated into several sets of advice from the Department of Health to the NHS.

Health service Circular (HSC) 1999/179 emphasises the importance of implementing existing guidance on the cleaning & sterilisation of medical devices[1]. It is complemented by a CD-ROM titled *Decontamination Guidance*, which draws together existing guidance on decontamination of medical equipment.

Health Service Circular HSC 2000/032 requires NHS organisations to review their management arrangements urgently and to carry out a health and safety audit of their decontamination procedures[2].

Systems that can track instrument sets through decontamination and use on patients are vital in identifying which instruments are used on a particular patient. Health Service Circular HSC 2000/032 also instructs trusts to set up such systems.

In addition to advising on the importance of effective decontamination, SEAC also advised that the use of single use instruments should be considered where practicable, provided patient safety is not compromised.

This advice is reiterated in HSC 1999/178. This describes the actions that health organisations and clinicians should take to reduce the risk of transmission[3].

Following the advice from SEAC, the Department of Health has introduced single-use instruments for tonsil surgery[4].

The Advisory Committee on Dangerous Pathogens (ACDP) advises government on health and safety risks from infectious diseases. A SEAC/ACDP Joint Working Group has been set up to advise on health and safety risks arising from CJD. This committee has issued advice on the measures to be taken when surgical interventions are carried out on patients with known or suspected CJD, or in one of the 'at risk' categories (3). This includes advice on the use and disposal of surgical instruments.

The Joint Working Group guidance considers the following groups to be potentially 'at risk ' of developing CJD: recipients of hormone derived from human pituitary glands e.g. growth hormone, gonadotrophin; recipients of dura mater grafts; people with a family history of CJD, i.e. close blood line relatives (parents, brothers, sisters, children, grandpartents and grandchildren).

1 Health service Circular (HSC) 1999/179 "*Controls Assurance in Infection Control: Decontamination of Medical Devices*"

2 Health Service Circular HSC 2000/032 "*Decontamination of medical devices*"

3 HSC 1999/178 "*Variant Creutzfeldt-Jakob Disease (vCJD): Minimising The Risk Of Transmission*"

4 Department of Health Announcement 04 January 2001

Three precautionary measures have been taken to reduce any potential risk of transmitting CJD through blood. First, people at risk of developing CJD are excluded from donating blood. Second, since April 1999, all major blood products (e.g. Factor VIII, immunoglobulins and anti-D for Rhesus negative pregnant women) have been manufactured from plasma donated outside the UK. Third, since October 1999 blood donated in the UK has been processed to remove its white blood cells (leucodepletion).

Annex 2: Instrument construction

The large majority of surgical instruments are manufactured from stainless steel. This can vary in quality (there are over 60 types of steel). Major European and USA manufacturers usually use high quality steel, but instruments of other origin may be made from lower grade steel which is difficult clean effectively.

The finish on an instrument can be polished or matt, and matt finished devices are more difficult to clean. Other materials such as aluminium, titanium and plastics can be part or the whole of an instrument structure. Aluminium and plastic are more difficult to clean than high grade stainless steel. Titanium devices should clean easily. Construction of devices varies from simple "single surface" to complex, multi-jointed or multi-part construction.

The following categorisation of instruments may help in considering how easily cleanable a particular instrument might be. Expert advice should be sought on instruments where category is not clear.

Instrument category	Examples of instruments
Category A: Can be decontaminated[5]	
Single-surface, no working parts	Macdonalds dissector, Deaver retractor
Jointed smooth jaws and no ratchet	Sinus forceps/scissors
Jointed with serrated jaws and ratchet	Spencer-Wells artery forceps
Multi-part instrument that can be dismantled into component parts	Balfour retractor
Category B: Varying degree of decontamination possible	
Multi-part/jointed instrument that cannot be fully dismantled	Compound action bone rongeur
Instruments with lumen	Minimal invasive surgery kit
Category C: Impossible to guarantee safe decontamination[6]	
Power tools(air or electric driven), not machine washable	Maxi-driver, Hall saw
Exotic kit with multi-part, multi-material, only partly strippable	Stereotactic neuro set
Fibre optic flexible scopes	
Instruments with lumen	neuro brain canula

5 If made from poor quality steel instruments may not be effectively decontaminated.

6 Some well-constructed kit in this category may be possible to decontaminate

Annex 3: Classification of specific procedures

Following advice from SEAC and various specialist subgroups, the following table classifies specific procedures according to whether they are normally liable to encounter potentially-infective tissues. These are defined as in the annual Hospital Episode Statistics, and shown with the standard "two letter" HES coding. Only procedures that would commonly have involved re-usable instruments are included.

Procedures encountering CNS (including pituitary and pineal glands) or posterior ophthalmic tissue

AA Tissue of brain

AB Ventricle of brain and subarachnoid space

AC Cranial nerves

AD Meninges of brain

AE Spinal cord and other contents of spinal canal
Excluding: Therapeutic epidural injection, Drainage of CSF, Therapeutic/Diagnostic spinal puncture, Spinal nerve root
i.e. **leaving only:** Partial extirpation of, Other open operations on, Other destruction of and Other operations on spinal cord; Repair of spina bifida; Other operations on meninges of spinal cord; Drainage of spinal canal – except of CSF

BA Pituitary and pineal glands

CA Orbit

CE Conjunctiva and cornea
Excluding: Subconjunctival injection

CF Sclera and iris
Excluding: Laser iridotomy

CH Retina and other parts of eye
Excluding: Cauterisation/Cryotherapy of lesion of retina, Laser photocoagulation of retina for detachment, Biopsy of lesion of eye nec, Repair of globe, Suture of eye nec, Removal of foreign body from eye nec, Fluorescein angiography of eye, Examination of eye under anaesthetic, Other

LC Carotid, cerebral and subclavian arteries
Excluding: Reconstruction/Other open/Transluminal operations on carotid artery, Transluminal operations on cerebral artery, Reconstruction/Other open/Transluminal operations on subclavian artery
i.e. **leaving only:** Operations on aneurysm of, and other Open operations on, cerebral artery

LG Veins and other blood vessels
Excluding: Arteriovenous shunt; Embolisation of Arteriovenous abnormality; Connection of vena cava (or branch of vc); Other bypass operations on/Repair of valve of vein; Other operations for venous insufficiency; Ligation of/Injection into varicose vein in leg; Open removal of thrombus from vein; Other vein related operations; Other open operations on vein; Therapeutic/Diagnostic transluminal operations on vein; Other operations on blood vessel
i.e. **leaving only:** Other arteriovenous operations except Embolisation of arteriovenous abnormality

VA Bones of cranium and face
Excluding: Plastic repair, Opening of cranium; 90% of other operations on cranium without elevation of depressed fracture; Excision of bone of face; Reduction of fracture of maxilla/other bone of face; Division/Fixation of other operations on bone of face; Excision of/Reduction of Fracture of (bones); Division of/Fixation of/Other operations on mandible; Reconstruction of/Other operations on temporomandibular joint
i.e. **Leaving only:** Elevation of depressed fracture of cranium, 10% of the remaining other operations on cranium (V05\V053)

Procedures encountering Anterior Eye tissue

CG Anterior chamber of eye and lens
Excluding: Capsulotomy of posterior lens capsule

Procedures encountering Lymphatic and equivalent risk tissue

BC Other endocrine glands

BD Breast

FD1 Excision of tonsil

FE Salivary apparatus

GA Oesophagus including hiatus hernia

GB Stomach pylorus & general upper gastrointestinal tract endoscopy

GC Duodenum

GD Jejunum

GE Ileum

HA Appendix

HB Colon

HC Rectum

JA Liver

JB Gall bladder

JC Bile duct

JD Pancreas

JE Spleen

MC Bladder

TG Lymphatic and other soft tissue

Provisionally excluded from any of the above categories:

A Nervous system

AE Operations on spinal nerve root,
Insertion of/attention to neurostimulator adjacent to spinal cord

AE Therapeutic epidural injection, Drainage of CSF,
Therapeutic/Diagnostic spinal puncture

AF Peripheral nerves

AG Other parts of nervous system

B Endocrine system and breast

BB Thyroid and parathyroid glands

C Eye

CB Eyebrow and eyelid

CC Lacrimal apparatus

CD Muscles of eye

CE Subconjunctival injection (C434)

CF Laser iridotomy (C623)

CG Capsulotomy of posterior lens capsule (C733)

CH Cauterisation/Cryotherapy of lesion of retina, Laser photocoagulation of retina for detachment, Biopsy of lesion of eye nec, Repair of globe, Suture of eye nec, Removal of foreign body from eye nec, Fluorescein angiography of eye, Examination of eye under anaesthetic, Other)

D Ear

DA External ear and external auditory canal

DB Mastoid and middle ear

DC Inner ear and Eustachian canal

E Respiratory tract

EA Nose

EB Nasal sinuses

EC Pharynx

ED Larynx

EE Trachea and bronchus

EF Lung and mediastinum

F Mouth

FA Lip

FB Tooth and gingiva

FC Tongue and palate

FD Tonsil and other parts of mouth **apart from** "FD1 Excision of tonsil"

H Lower digestive tract

HD Anus and perianal region

K Heart

KA Wall septum and chambers of heart

KB Valves of heart and adjacent structures

KC Coronary artery

KD Other parts of heart and pericardium

L Arteries and veins

LA Great vessels and pulmonary artery

LB Aorta

LC Reconstruction/Other open/Transluminal operations on carotid artery, Transluminal operations on cerebral artery, Reconstruction/Other open/transluminal operations on subclavian artery

LD Abdominal branches of aorta

LE Iliac and femoral arteries

LF Other arteries

LG Arteriovenous shunt; Embolisation of Arteriovenous abnormality; Connection of vena cava; Other bypass operations on/repair of valve of vein; Other operations for venous insufficiency; Ligation of/injection into varicose vein in leg; Open removal of thrombus from vein; Other vein related operations; Other open operations on vein; Therapeutic/Diagnostic transluminal operations on vein; Other operations on blood

M Male Urinary

MA Kidney

MB Ureter

MD Outlet of bladder and prostate

ME Urethra and other parts of urinary tract

N Male genital organs

NA Scrotum and testis

NB Spermatic cord and male perineum

NC Penis and other male genital organs

P Lower female genital tract

PA Vulva and female perineum

PB Vagina

Q Upper female genital tract

QA Uterus

QB Fallopian tube

QC Ovary and broad ligament

R Female genital tract associated with pregnancy, birth & puerperium

RA Foetus gravid uterus

RB Induction and delivery

RC Other obstetric

S Skin

SA Skin or subcutaneous tissue

SB Nail

T Soft tissue

TA	Chest wall pleura and diaphragm
TB	Abdominal wall
TC	Peritoneum
TD	Fascia, ganglion and bursa
TE	Tendon
TF	Muscle

V Bones and joints of skull and spine

VA	90% of Other operations on cranium without Elevation of depressed fracture (90% V05\V053)
VA	Remaining Bones of cranium and face
VB	Jaw and temporomandibular joint
VC	Decompression operations on spine
VD	Operations on intervertebral disc
VE	Other operations on spine

W Other bones and joints

WA	Complex reconstruction of hand and foot
WB	Graft of bone marrow (W34)
WB	Other Bone (Excluding Graft of bone marrow)
WC	Joint

X Miscellaneous operations

XA	Operations covering multiple systems
XB	Miscellaneous operations

Annex 4: Reporting form for possible exposures to CJD through medical procedures

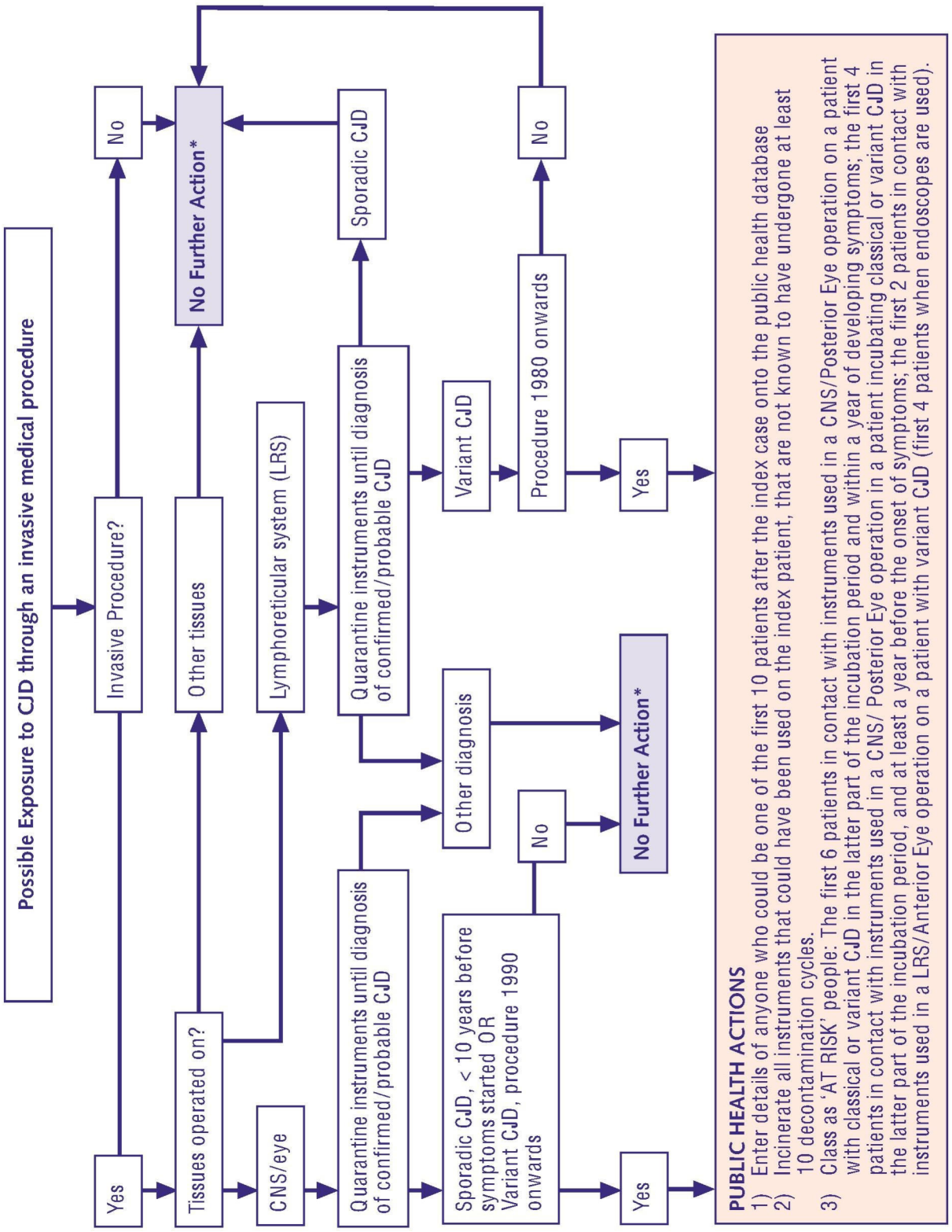
Please complete this form for all invasive medical procedures.

Please report all possible exposures to Pip Edwards at the Department of Health on GRO-C
Please send this form to her by fax on GRO-C, or by e-mail at Philippa.edwards@ GRO-C

DH team member contacted	Date	PI
Your details (name, position)		
Organisation (address)		
Telephone/fax/email contact details		
Patient's name		
CJD diagnosis (please tick box)	possible	probable	confirmed
sporadic	☐	☐	☐
variant	☐	☐	☐
familial	☐	☐	☐
iatrogenic	☐	☐	☐
If diagnosis has not been confirmed, please give supporting details		
Who made the diagnosis (NCJDSU, local neurologist etc.)		
Date of onset of symptoms of CJD		

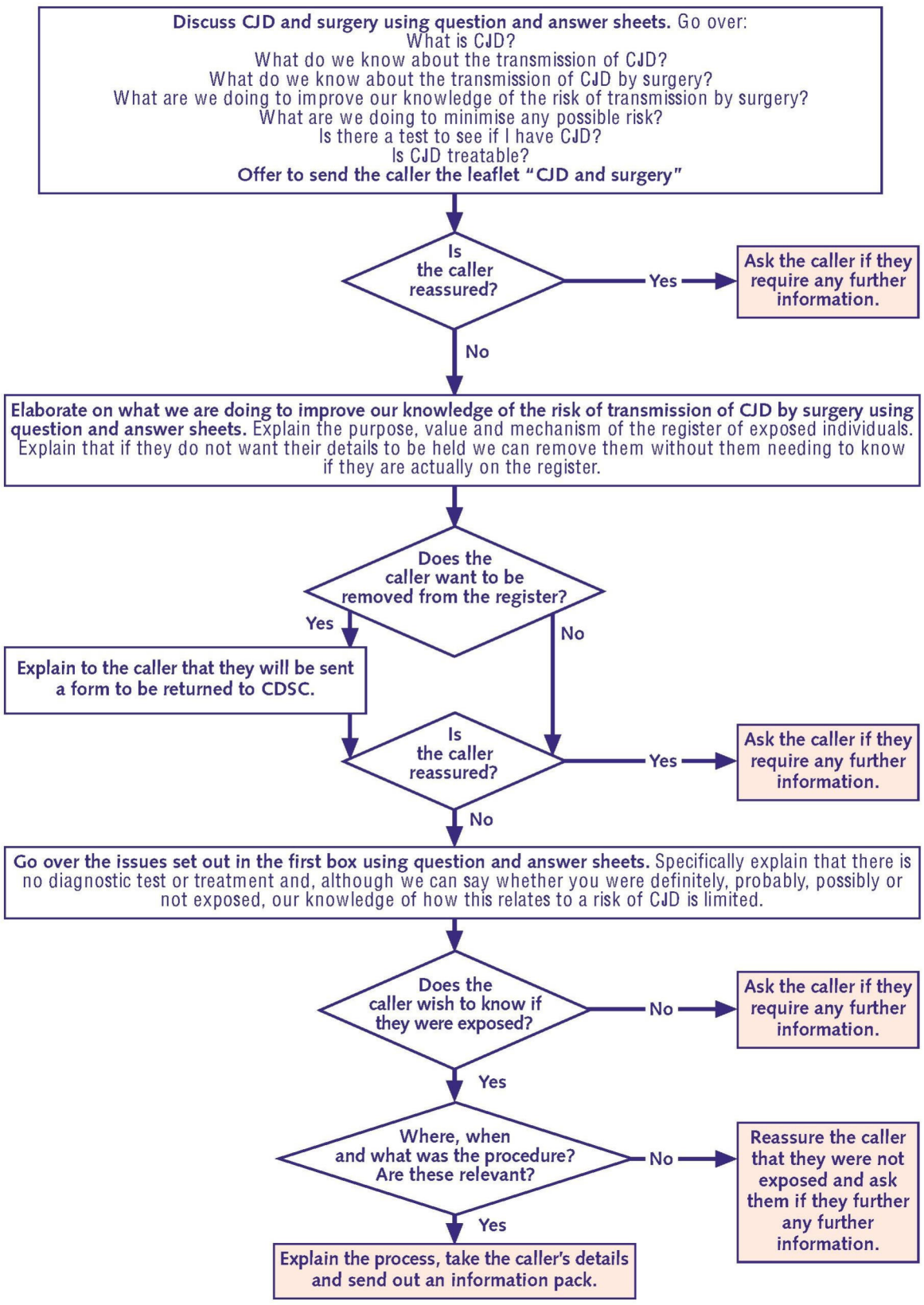
Possible exposure (please use a new page for each procedure)	
Date of procedure	
Description of procedure	
Tissues involved	
Anaesthetic procedures	
Clinical reason why the procedure was required (for surgical procedures)	
Was an endoscope used? (please tick box)	Yes ☐ No ☐

Annex 5: Possible exposure to CJD through an invasive medical procedure



* Clean and sterilise instruments according to guidance and return to use. No other action required.

Annex 6


Discuss CJD and surgery using question and answer sheets. Go over:
What is CJD?
What do we know about the transmission of CJD?
What do we know about the transmission of CJD by surgery?
What are we doing to improve our knowledge of the risk of transmission by surgery?
What are we doing to minimise any possible risk?
Is there a test to see if I have CJD?
Is CJD treatable?
Offer to send the caller the leaflet "CJD and surgery"
Is the caller reassured?
Yes
Ask the caller if they require any further information.
No
Elaborate on what we are doing to improve our knowledge of the risk of transmission of CJD by surgery using question and answer sheets. Explain the purpose, value and mechanism of the register of exposed individuals. Explain that if they do not want their details to be held we can remove them without them needing to know if they are actually on the register.
Does the caller want to be removed from the register?
Yes
No
Explain to the caller that they will be sent a form to be returned to CDSC.
Is the caller reassured?
Yes
Ask the caller if they require any further information.
No
Go over the issues set out in the first box using question and answer sheets. Specifically explain that there is no diagnostic test or treatment and, although we can say whether you were definitely, probably, possibly or not exposed, our knowledge of how this relates to a risk of CJD is limited.
Does the caller wish to know if they were exposed?
No
Ask the caller if they require any further information.
Yes
Where, when and what was the procedure? Are these relevant?
No
Reassure the caller that they were not exposed and ask them if they further any further information.
Yes
Explain the process, take the caller's details and send out an information pack.

Glossary

ACDP	Advisory Committee on Dangerous Pathogens, established in 1981 to advise the Health and Safety Executive on all aspects of hazards and risks to workers and others from exposure to pathogens.
BSE	Bovine Spongiform Encephalopathy, a slowly progressive and ultimately fatal neurological disorder of adult cattle transmitted by contaminated animal feed.
CDSC	Communicable Disease Surveillance Centre. Responsible for monitoring human infectious diseases.
CJD	Creutzfeldt-Jakob Disease, a human transmissible spongiform encephalopathy that can occur in sporadic, familial and acquired (iatrogenic) forms.
Cleaning	A process which physically removes contamination but does not necessarily destroy micro-organisms.
CNS	Central nervous system. This includes the brain, cranial nerves and spinal cord.
Contactable Patients	People exposed in an incident who are are considered to have a higher risk of acquiring CJD. They should be contacted and informed about their exposure so that action may be taken to prevent any further spread of disease.
CSF	Cerebrospinal fluid, the fluid that bathes the brain and spinal cord.
Decontamination	A process which removes or destroys contamination and thereby prevents micro-organisms or other contaminants reaching a susceptible site in sufficient quantities to initiate infection or any other harmful response.
Definite case of CJD	An international definition used by the CJD Surveillance Unit that refers to the diagnostic status of cases. In definite cases the diagnosis will have been pathologically confirmed, in most cases by post mortem examination of brain tissue (rarely it may be possible to establish a definite diagnosis by brain biopsy while the patient is still alive).
Dose response relationship	This describes how the amount of an infectious agent affects the likelihood that an exposed individual becomes infected.
Dura mater	The outermost and strongest of the three membranes (meninges) which envelop the brain and spinal cord.
Endoscopes	Tube-shaped instruments inserted into a cavity in the body to investigate and treat disorders. There are many types of endoscopes e.g. arthroscopes, laparoscopes, cyctoscopes, gastroscopes, colonoscopes and bronchoscopes.

Familial CJD

CJD cases that occur in families, associated with mutations in the PrP gene (10 – 15% of all CJD cases).

HGH

Human growth Hormone. At one time made from pituitaries from human cadavers. This was rarely contaminated with CJD agent, and is now known to have transmitted CJD to a number of those treated with hGH for short stature.

Iatrogenic CJD

Infection with CJD that occurred as the result of a medical procedure. Recent UK cases have resulted from treatment with human derived pituitary growth hormones or from grafts using dura mater (a membrane lining the skull).

Lymphoreticular system (LRS)

Lymphoreticular System is referred to because of its possible infectivity in variant CJD. Infectivity has been demonstrated in the lymph nodes, appendiceal lymphatic tissue, spleen and tonsils in variant CJD.

Median infective dose (ID_{50})

The statistically derived single dose of a infective agent that can be expected to cause infection in 50 per cent of a given population of organisms under a defined set of experimental conditions.

Medical device

An instrument, apparatus, appliance, material or other article, whether used alone or in combination together with any accessories or software necessary for its proper functioning, intended by the manufacturer to be used for human beings in the:

diagnosis, prevention, monitoring, treatment or alleviation of disease or injury; investigation, replacement or modification of the anatomy or of a physiological process; control of conception;

and which does not achieve its principal intended action by pharmacological, chemical, immunological or metabolic means, but which may be assisted in its function by such means.

NCJDSU

The National CJD Surveillance Unit was established in Edinburgh in 1990, to identify and study all cases of CJD in the UK.

Possible case of CJD

An international definition used by the CJD Surveillance Unit that refers to the diagnostic status of cases. Possible cases fulfil certain clinical criteria, but do not meet the criteria for probable or definite cases.

Prion

PROteinaceous INfectious agent. The prion theory suggests that the infective agent of CJD (and the other TSEs) is only composed of a protein and does not contain nucleic acid which would be necessary if the agent was a conventional virus.

Prion protein (PrP)

Protease-resistant membrane protein, also known as prion protein (PrP): a normal, host-coded protein that becomes protease-resistant in infected tissue and accumulates around CNS lesions in TSEs. Until recently, the function of PrP was unknown despite its presence in many different organs and tissues of healthy animals, including the brain. There is recent evidence that PrP in uninfected animals has the property of mopping up harmful 'oxygen free radicals' or carries out some signalling functions between cells.

Probable case of CJD	An international definition used by the CJD Surveillance Unit that refers to the diagnostic status of cases. Probable cases fulfil clinical criteria but do not meet the criteria for definite cases.
Prophylactic	Treatments used to prevent infection or disease.
PrP^{C}	The normal cellular isoform of PrP.
PrP^{Sc}	The abnormal disease-specific isoform of PrP derived post-translationally from PrP^{C}. PrP^{Sc} is a generic term now used for all disease-associated PrP.
Scrapie	A TSE endemic in British sheep and found in many parts of the world. It is also found in goats. Scrapie can be transmitted naturally or experimentally to other animals such as mice and this provides an experimental model for work on TSEs.
SEAC	Spongiform Encephalopathy Advisory Committee. This was established in April 1990 to advise government on matters related to Spongiform Encephalopathies.
Single Use Device	Any device deemed unsuitable by the manufacturer for re-processing.
Sporadic CJD	Cases of CJD that occur at random throughout the world and have no known cause. This is the commonest form of CJD.
TME	Transmissible mink encephalopathy. This is a TSE of minks that has been found in mink farms in the USA, probably resulting from dietary exposure to scrapie.
Transmissible Spongiform Encephalopathy (TSE)	Transmissible spongiform encephalopathy. Fatal diseases of the neurological system characterised by spongy degeneration of the brain with progressive dementia. Examples include CJD in humans, and scrapie and BSE in animals
Variant CJD	Identified in 1996 as a previously unrecognised form of CJD, having a novel pathology and consistent disease pattern. Exposure to BSE is the most likely explanation for the emergence of the disease. It was previously known as nvCJD (new variant CJD).

Panel members

-----Copy to be supplied------

Reporting form for possible exposures to CJD through medical procedures

Please complete this form for all invasive medical procedures.

Please report all possible exposures to Pip Edwards at the Department of Health on GRO-C.
Please send this form to her by fax on GRO-C, or by e-mail at Philippa.edwards@GRO-C.

DH team member contacted	Date	PI
Your details (name, position)		
Organisation (address)		
Telephone/fax/email contact details		
Patient's name		
CJD diagnosis (please tick box)	possible	probable	confirmed
sporadic	☐	☐	☐
variant	☐	☐	☐
familial	☐	☐	☐
iatrogenic	☐	☐	☐
If diagnosis has not been confirmed, please give supporting details		
Who made the diagnosis (NCJDSU, local neurologist etc.)		
Date of onset of symptoms of CJD		

Possible exposure (please use a new page for each procedure)	
Date of procedure	
Description of procedure	
Tissues involved	
Anaesthetic procedures	
Clinical reason why the procedure was required (for surgical procedures)	
Was an endoscope used? (please tick box)	Yes ☐ No ☐

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