PROTOCOL

Surveillance of CJD in the UK

NATIONAL CREUTZFELDT-JAKOB DISEASE
RESEARCH & SURVEILLANCE UNIT (NCJDRSU),
UNIVERSITY OF EDINBURGH

Sponsors	University of Edinburgh
Funder	Department of Health and Scottish Government Policy Research Programme
Funding Reference Number	PR-ST-0614-0008
Address	National CJD Research & Surveillance Unit Bryan Matthews Building, Western General Hospital, Crewe Road, Edinburgh, EH4 2XU, UK
Director	Dr AJE Green
Version Number and Date	Version 4, April 2017

CONTENTS

LIST OF ABBREVIATIONS

CJD	Creutzfeldt-Jakob Disease
TSE	Transmissible Spongiform Encephalopathy
BSE	Bovine Spongiform Encephalopathy
sCJD	Sporadic Creutzfeldt-Jakob Disease
vCJD	Variant Creutzfeldt-Jakob Disease
iCJD	Iatrogenic Creutzfeldt-Jakob Disease
gCJD	Genetic Creutzfeldt-Jakob Disease
FFI	Fatal Familial Insomnia
GSS	Gerstmann-Straussler-Scheinker Syndrome
vPSPr	Variably Protease Sensitive Prionopathy
NCJDRSU	National Creutzfeldt-Jakob Disease Research & Surveillance Unit
NPC	National Prion Clinic
TMER	Transfusion Medicine Epidemiology Review
PIND	Study of Progressive Intellectual & Neurological Deterioration
NHSBT	National Health Service Blood and Tranplant
PHE	Public Health England
HPS	Public Health Scotland
EU	European Union
CDC	Centers for Disease Control and Prevention
CNS	Central Nervous System
PRNP	PRioN Protein
PrP^{res}	Protease-resistant prion protein

SUMMARY

Following the identification in UK cattle of bovine spongiform encephalopathy (BSE) as one of the transmissible spongiform encephalopathies (TSEs), the Southwood Report recommended that Creutzfeldt-Jakob disease (CJD) should be monitored. The National Creutzfeldt-Jakob Disease Research & Surveillance Unit (NCJDRSU) was established in 1990 with the primary aim of identifying any changes in the characteristics of CJD that might be linked to BSE. In 1996, a new variant of CJD (vCJD) was identified and evidence has since gathered that links vCJD causally to BSE. The exact mechanism of transmission of the BSE agent to the human population has not been identified, but dietary exposure to BSE contaminated beef products remains the most likely hypothesis.

1 INTRODUCTION

1.1 Disease

Prion diseases are a very rare group of neurodegenerative diseases which are all currently untreatable and ultimately fatal. Prion diseases can exist in different forms, but the most common is sporadic CJD (sCJD) and occurs worldwide causing around 1-2 deaths per million population per annum. There are also inherited forms of human prion disease linked to mutations of the prion protein gene (gCJD, FFI, GSS) and cases caused by transmission via medical or surgical treatments (iCJD).

1.2 Background and Rationale

CJD was first described by Hans Creutzfeldt, a German neuropathologist, and Alfons Jakob, a German neurologist who worked in the field of neuropathology, in the early 1920s. Following the identification in UK cattle of BSE, the Southwood Committee was set up to look at all aspects of the disease, including any human health implications. One of the recommendations of the Southwood Committee Report, published in 1989, was that CJD should be monitored to identify any changes in the characteristics of CJD that might be linked to BSE. As a result, the NCJDRSU was established in 1990 to carry out surveillance of CJD in the UK. In 1996, a new variant of CJD (vCJD) was identified and evidence since gathered links vCJD causally to BSE. The exact mechanism of transmission of the BSE agent to the human population has not been identified, but dietary exposure to BSE contaminated beef products remains the most likely hypothesis.

2 AIMS & OBJECTIVES

2.1 Aims

The primary aim of CJD surveillance in the UK is to inform the scientific community, policy makers and, ultimately, the general public of changes in the epidemiology of prion diseases in general and in particular CJD and vCJD and of potential risk factors, in order to plan for and reduce the potential consequences of this disease.

2.2 Objectives

The objectives of the NCJDRSU are to identify all cases of CJD in the UK and to investigate each case further by clinical examination, clinical investigations, neuropathological examination, genetic analysis, molecular biological studies and collecting basic epidemiological data in order to:

- provide accurate data on the incidence of CJD, including vCJD;
- provide estimates of short-term and long-term trends in the rate of occurrence of vCJD;
- investigate the mechanism of transmission of BSE to the human population;
- investigate risk factors for CJD, including vCJD;
- evaluate the potential risks of onward transmission of vCJD, including through iatrogenic routes;
- identify any novel forms of human spongiform encephalopathy;
- evaluate case definitions of CJD, including vCJD; and
- evaluate diagnostic tests for CJD, including vCJD.

3 DESIGN

3.1 Routine Surveillance

3.1.1 Referral

Referral of suspect cases to the NCJDRSU can occur in several ways:
Clinical – passive ascertainment: neurologists or neuropathologists who refer any individuals in whom CJD or vCJD is considered a possible diagnosis to the NCJDRSU.
Death Certificates – passive ascertainment: the Office for National Statistics for England and Wales and the General Register Offices for Scotland and Northern Ireland supply all death certificates coded under rubrics A81.0 (**Creutzfeldt-Jakob disease** Incl.: Subacute spongiform encephalopathy) and F02.1 (**Dementia in Creutzfeldt-Jakob disease)** (10^{th} ICD Revision).
Other Sources – passive ascertainment: psychiatrists, paediatricians (also active surveillance, see below), geriatricians, other health professionals and members of the general public may refer cases to NCJDRSU.

The current national reporting system was announced by the Chief Medical Officer in July 2004. This is centred on a National CJD Reporting Form available to facilitate this process, to be sent, by the notifying clinician, to the NCJDRSU, the National Prion Clinic (NPC) and the local Consultant in Health Protection/Public Health (CPHMs, CCDCs) (Appendix 1).

When a new or suspect case is first referred to the NCJDRSU, a unique NCJDRSU number is allocated and a patient file is created. The NCJDRSU will also notify NPC of the referral. This system does not preclude the possibility of a clinician informally discussing a suspect or doubtful case with the NCJDRSU or NPC. The NCJDRSU are very happy to discuss cases and provide clinical and other advice concerning potential cases of CJD.

The NCJDRSU continues to provide a national CJD diagnostic CSF 14-3-3 service and will arrange courier collection of CSF samples and prompt results.

In August 2012 the NCJDRSU published results from a retrospective study investigating a new technique for examining CSF samples from patients with suspected CJD, called Real-Time Quaking Induced Conversion (RT-QuIC). The results were very promising and since that time, NCJDRSU have been undertaking a prospective audit of how useful RT-QuIC is in clinical practice, therefore every CSF sample that is sent for 14-3-3 analysis from UK patients is also analysed for RT-QuIC[1], providing enough CSF is available.

3.1.2 Classification

Suspect cases are classified according to published criteria (Appendix 2). This is an on-going process, being constantly updated as more information about the diagnosis becomes available. The date of any change of classification and the reason for that change is recorded on the *Change in Classification Form* (Appendix 3). In addition, the classification is recorded at the following key stages:

[1] not part of surveillance per se

- at notification
- when the suspect case was first seen in life by a neurologist from NCJDRSU
- the highest classification on the basis of clinical information alone (ie not including neuropathological information)
- when review by NCJDRSU is complete (ie when the case-file is 'closed')

3.1.3 Follow Up of Suspect Cases

Whenever possible, all referrals to the NCJDRSU categorised as 'definite CJD', 'probable CJD', 'possible CJD' and 'diagnosis unclear' are visited in life in order to carry out a physical examination and to gather systematic clinical information from the suspect case and their relatives. The relatives are given an Information Sheet detailing information about the project and they are asked to sign a Consent Form agreeing to be interviewed and giving their consent for the NCJDRSU to access medical and dental records (Appendix 4). During such visits, an NCJDRSU neurologist examines the patient and completes Sections 3 and 4 of the *Clinical and Epidemiological Review* form (Appendix 5). At the same visit, a close relative or nominated spokesperson is interviewed by either the neurologist or a nurse from the NCJDRSU who completes Sections 1 and 2 of the *Clinical and Epidemiological Review* form and, for variant cases only, *Beef Purchasing Questionnaire* (Appendix 6).

Following this visit the NCJDRSU neurologist will write to the local clinician (copied to the patient's GP and the NPC) outlining their clinical formulation and diagnostic classification according to the defined criteria (Appendix 2). Letters will also be sent to the relevant departments of the referring hospital to request copies of hospital notes, MRI scans and EEG tracings. Finally, a letter will be sent to the patient's relative or spokesperson to thank them for agreeing to the visit and reiterating information given to them at the visit about NCJDRSU and the study, reassuring them about confidentiality and providing contact numbers for the NCJDRSU for any follow up questions.

Following the death of a suspect case and if a post mortem is performed, every effort is made to obtain details of the report and review of any pathological material is organised. Where material is reviewed, or post mortem performed by the NCJDRSU neuropathologist, a copy of the NCJDRSU neuropathologist's report will be sent to the local clinician in charge of the patient's care as well as the referring pathologist. In addition, the general practice records are requested and used to complete the *GP Medical History Form* (Appendix 7).

If referral to the NCJDRSU is made after death or death occurs soon after referral and before a visit can be undertaken, an attempt is made to visit the relatives of the case after an appropriate period of time in order to gather further epidemiological information (using Sections 1 and 2 of the *Clinical and Epidemiological Review* form, Appendix 5) and hospital and GP notes are requested, along with copies of MRI and EEG (from which data will be extracted into Sections 3 and 4 of the *Clinical and Epidemiological Review* form, Appendix 5 and *GP Medical History Form,* Appendix 7*)*.

Where a case is identified only when a death certificate coded under the rubric for CJD or other CJD is received, efforts will be made to ascertain where the diagnosis was made and clinical and/or pathological information requested. If further

information indicates that the case could be classified as probable or definite CJD, an attempt will be made to visit the relatives of the case as detailed above.

Changes in diagnostic criteria that occur as data are accrued in relation to suspect cases of CJD are noted on the *Change of Classification Form* (Appendix 3).

Referrals classified as probable or definite genetic CJD or accidentally transmitted TSE (also known as iatrogenic CJD) are not followed up by NCJDRSU, unless the diagnosis is unclear or a specific request is made by the local clinician for a visit by a neurologist from NCJDRSU. The Institute of Child Health, London follows up cases of growth hormone related iatrogenic CJD and the investigation of cases of genetic CJD is undertaken by the National Prion Clinic, London.

3.1.4 Cessation of Follow Up

In order to obtain as much complete data on each case as is possible, following the death of a suspect case (or following recovery), the files are reviewed twice yearly. When it is apparent that no further clinical, pathological or other laboratory data are likely to be forthcoming, the case file is closed.

3.2 Public Health Reporting

The NCJDRSU neurologist will ask the local clinician to complete a *Public Health Reporting Form* (Appendix 8) to be sent to their local health protection team and will encourage them to also notify their local infection control team.

To support the public health follow-up, the NCJDRSU will also inform the local health protection team of the diagnosis, and information may be shared in confidence with the public health professionals to prevent any possible spread of CJD between people. This is vital, as patients with CJD may have had surgery, or donated blood or other tissues, and a local response may be required to help prevent spread.

3.3 Geographically Associated Cases of CJD

It is imperative that there is a co-ordinated standard approach when investigating a potential cluster or connection between cases of vCJD. According to the National Protocol for the Investigation of Geographically Associated Cases of vCJD (http://www.media.is.ed.ac.uk/builds/cjd/documents/gac.pdf), this approach will be led locally and involves a close collaboration between the NCJDRSU, the public health agency concerned (Public Health England, Health Protection Scotland, Public Health Wales or Public Health Agency Northern Ireland), the regional epidemiologist, local public health representative, environmental health and veterinary specialists and local clinicians. A similar approach should also be considered for sCJD.

3.4 Enhanced Surveillance

3.4.1 Paediatric surveillance

(Study of Progressive Intellectual & Neurological Deterioration [PIND])

This is carried out through prospective active surveillance in conjunction with the British Paediatric Surveillance Unit. The aim is to identify cases of progressive

intellectual and neurological deterioration and to determine whether or not cases of CJD are occurring in children resident in the UK aged under 16 years at onset of symptoms.

3.4.2 Reporting of blood donation and transfusion history

(Transfusion Medicine Epidemiology Review [TMER])

Variant CJD: As soon as a suspect case is classified as 'probable vCJD', the Medical Director(s) of all UK blood services (England, Scotland, Wales and Northern Ireland) are notified with the following information: forename, surname, maiden name, sex, date of birth, residential history, whether a donor, donation dates, places of donation, vCJD classification (Appendix 9). An anonymised copy is sent to the Department of Health in each country. If the suspect case has a known history of blood transfusion, the Medical Director of NHSBT is given details of where and when the transfusion was carried out.

Sporadic CJD: NHSBT is informed on a six monthly basis of all definite and probable cases of sporadic and genetic CJD who were reported as blood component donors ('main TMER') and those who were reported as blood component recipients ('reverse TMER'). Basic information sent in relation to donors includes name, maiden name, sex, date of birth, year of donation(s), the home address at time of donation(s) and where donation(s) was/were given. For blood component recipients the information sent includes name, maiden name, sex, date of birth, date of transfusion(s), the home address at the time of transfusion(s), the hospital where the transfusion(s) occurred and the indication for the transfusion(s). Similar details for controls are also given and the information sent is 'blinded' with regards to whether it relates to cases or controls.

3.4.3 Surveillance of potential occupational exposure to CJD

This is a collaboration between NCJDRSU, Public Health England (PHE) and Heath Protection Scotland (HPS). As NCJDRSU investigates the occupational history of all CJD cases, PHE/HPS and NCJDRSU have developed a joint system for identifying, investigating and recording significant occupational exposures to TSEs and for monitoring outcomes of those exposures.

The study has two parts. 1) a registry for the prospective long term monitoring of healthcare and laboratory workers who have incurred occupational exposures to TSEs and 2) the retrospective review of possible occupational exposures of CJD cases who have been healthcare or laboratory workers.

The prospective element of the registry involves voluntary reporting of occupational exposures as they occur. The healthcare and laboratory workers can provide consent to inclusion on the registry for long term follow up to ascertain whether they ever go on to develop signs or symptoms of prion infection.

In the retrospective element, for CJD patients who have been healthcare workers, overlaps between their employment and all hospital procedures and inpatient stays of other CJD patients are identified. These time and place overlaps indicate 'potential exposure periods'. If any such periods are identified, a further investigation with the

hospital can be undertaken to identify any possible occupational links between the CJD infected healthcare worker and the concurrent CJD patient.

For CJD patients who have been laboratory workers, investigations are conducted with the relevant workplace to identify any possible exposures and accidental injuries involving TSE infected animals or tissues during their employment.

3.4.4 Enhanced surveillance of individuals identified as at increased risk of CJD

NCJDRSU collaborates with Public Health England (PHE) and Health Protection Scotland (HPS) who carry out surveillance of individuals at increased risk of CJD due to healthcare exposures. Individuals in at-risk groups have experienced a range of exposures and probably have different risks of infection. On a 6-monthly basis, NCJDRSU are sent a list of at-risk individuals from PHE and these individuals are cross-checked with the NCJDRSU database of cases of definite or probable CJD.

4 Recommended Minimum Data Elements

The following minimum data sets are collected:

4.1 Notification Form

Identification information, notification details, history, examination at notification, risk factors, classification at notification.

4.2 Change in Classification Form

For each change in classification: classification, criteria for classification, date of change and reason for change.

4.3 Clinical and Epidemiological Review form

Sections 1 and 2 Identification information, epidemiological information gathered from patient's relative/spokesperson regarding past medical and dental history, residential history, occupational history, educational history, family history, dietary history, social contact with any other person suffering from CJD and exposure to animals. Sections 3 and 4 Examination review, clinical history, treatment (if applicable) and review of investigations (including EEG, MRI, CSF 14-3-3).

4.4 Neuropathology in cases where post mortem has been performed

Post mortem report with the referring pathologist's diagnosis and any other relevant findings at autopsy. Review of the neuropathological material includes PrP immunocytochemistry and investigations on non-central nervous system (CNS) tissues, including lymphoid and peripheral nervous system tissues. All referring pathologists are encouraged to freeze CNS and other tissues for biochemical studies (prion protein (PrP^{res}) typing) and, when necessary, DNA extraction (for prion protein gene (*PRNP*) analysis in which consent for genetic analysis is obtained).

5 Recommended Data Analysis, Presentations,

5.1 By case of vCJD

Once relatives and local clinicians have been informed of the diagnosis of definite or probable vCJD, the NCJDRSU informs the following by email giving details of sex, age, vCJD classification, whether the patient is alive or dead and the total number of vCJD cases in the UK: Departments of Health in the UK, colleagues in the EU surveillance system, CDC Atlanta, European Commission, CJD Support Group and other interested parties.

5.2 Monthly

Number of referrals for investigation; numbers of sporadic, iatrogenic, genetic and vCJD cases by year of death are sent to Department of Health and posted on the NCJDRSU website.

5.3 Annually

NCJDRSU Annual Report

This report contains the following minimum information:

- *Sporadic CJD*

  Number of referrals per annum to NCJDRSU; mortality rates and age-specific mortality rates over the years of the study including retrospective studies and standardised mortality ratios by region; geographical distribution of sCJD.
- *Variant CJD*

  Summary of number of cases and characteristics (mean age at onset, etc); age- and sex-specific mortality rates; standardised incidence ratios by region; geographical distribution of vCJD.
- *Summary Results from the following:*

  Iatrogenic CJD; TMER; PIND; surveillance of potential exposure to CJD; enhanced Surveillance of CJD.
- *Laboratory Activities*

  Statement of progress and surveillance activities; prion protein laboratory results; brain banking activities; molecular genetics; CSF 14-3-3 and other brain specific proteins.
- *National Care Team*
- *Publications*
- *Staff based at NCJDRSU*

5.4 Websites

Information is regularly posted and updated on the NCJDRSU website (www.cjd.ed.ac.uk) and the CJD International Surveillance Network (www.eurocjd.ed.ac.uk).

5.5 Ad hoc

As requested.

5.6 Principal uses of data for decision making

- develop and test hypotheses about novel forms of spongiform encephalopathy;
- track trends over time;
- detect clusters;
- detection of risk factors and mechanisms of transmission;
- determine magnitude of public health problem;
- inform prevention strategies;
- development and evaluation of diagnostic tests.

5.7 Special Aspects

Collaboration with surveillance units within the EU and world-wide.

6 ETHICAL CONDUCT

Surveillance will be conducted in accordance with the principles of the International Conference on Harmonisation Tripartite Guideline for Good Practice (ICH GCP). Ethical approval is not required (Appendix 10).

7 REFERENCE SECTION

1. Creutzfeldt HG. Uber eine eigenartige herdformige Erkrankung des Zentralnervensystems. Z ges Neurol Psychiat 1920; 57: 1-18.

2. Jakob A. Uber eine der multiplen sklerose klinisch nahenstehende erkrankung des zentralnervensystems (spastiche pseudosklerose) mit bemerkswertem anatomishen befunde. Medizinische Klinik 1921; 13: 372-376.

3. Southwood Committee. Report of the Working Party on Bovine Spongiform Encephalopathy. 1989. ISBN 1851974059.

4. Will RG, Ironside JW, Zeidler M, Cousens SN, Estibeiro K, Alperovitch A, Poser S, Pocchiari M, Hofman A, Smith PG. A new variant of Creutzfeldt-Jakob disease in the UK. Lancet 1996; 347: 921-925.

5. Bruce ME, Will RG, Ironside JW, McConnell I, Drummond D, Suttie A, McCardle L, Chree A, Hope J, Birkett C, Cousens S, Fraser H, Bostock CJ. Transmissions to mice indicate that 'new variant' CJD is caused by the BSE agent. Nature 1997; 389: 498-501.

6. Budka H, Aguzzi A, Brown P, Brucher J-M, Bugiani O, Collinge J, Diringer H, Gullotta F, Haltia M, Hauw J-J, Ironside JW, Kretzschmar HA, Lantos PL, Masullo C, Pocchiari M,

Schlote W, Tateishi J, Will RG. Tissue handling in suspected Creutzfeldt-Jakob disease (CJD) and other human spongiform encephalopathies (prion diseases). Brain Pathology 1995; 5: 319-322.

7. Will RG, Stewart G, Zeidler M, Macleod MA, Knight RSG. Psychiatric features of new variant Creutzfeldt-Jakob disease. Psychiatric Bulletin 1999; 23: 264-267.

8. Ironside JW, Sutherland K, Bell JE, McCardle L, Barrie C, Estibeiro K, Zeidler M, Will RG. A new variant of Creutzfeldt-Jakob disease: neuropathological and clinical features. Cold Spring Harbour Laboratory Press 1996; 523-530.

10. Llewelyn CA, Hewitt PA, Knight RSG, Amar K, Cousens S, Mackenzie J, Will RG. Possible transmission of variant Creutzfeldt-Jakob disease by blood transfusion. Lancet 2004; 363: 417-421.

APPENDIX 1

National Referral System: NATIONAL CJD REPORTING FORM

last updated April 2012

FAX TO:

Patient details

Surname:..... Forename(s):.....

Postal Address:.....
.....
.....
Postcode:.....

Telephone number:.....

Fax Number:.....

Email Address:.....

NHS Number, if known:.....

Family, carer or independent representative details (if appropriate*)

** This may be appropriate if the approach is made via a lead family member, carer or independent representative (i.e. when a patient is too ill to be approached directly or has a preference for this route).*

Surname:..... Forename(s):.....

Postal Address:.....
.....
.....
Postcode:.....

Telephone number:.....

Fax Number:.....

Email Address:.....

Neurologist details (or other hospital clinician)

Surname:..... Forename(s):.....

Hospital Postal Address:.....
.....
.....
Postcode:.....

Telephone number:.....
Fax Number:.....

CCDC details

Surname:..... Forename(s):.....

Postal Address:.....
.....
Postcode:.....

Telephone number:.....

GP Details

Surname:..... Forename(s):.....

GP Practice Postal Address:.....
.....
.....
Postcode:.....

Telephone number:.....
Fax Number:.....

Brief clinical details: (please attach recent letter or discharge summary)

.....

.....

.....

.....

.....

Consent:
*please delete as appropriate

I have been provided with the patient information leaflet which explains the role of the National CJD Research & Surveillance Unit and the National Prion Clinic.	YES / NO
I agree to my/the patient's* details being forwarded to the National CJD Research & Surveillance Unit and the National Prion Clinic.	YES / NO
I agree that staff from the National CJD Research & Surveillance Unit in Edinburgh and the National Prion Clinic in London can visit myself/the patient* and my/their* relatives at a mutually convenient time for clinical assessment and surveillance purposes and to provide the opportunity, should we wish, to discuss ongoing research, including clinical trials of potential treatments.	YES / NO
I understand that this may mean providing further information to help in the organisation of my/the patient's* care, and to contribute to a better understanding of the illness.	YES / NO

Signed: .....

Print: .....

Date: .....

On completion, please fax securely to NCJDRSU 0131 343 1404, NPC 0203 448 4046 and also to your local CCDC

APPENDIX 2

DIAGNOSTIC CRITERIA

1. SPORADIC CJD (from January 2017)

1.1 **DEFINITE:**

Progressive neurological syndrome **AND**

Neuropathologically **or** immunocytochemically

or biochemically confirmed

1.2 **PROBABLE:**

1.2.1 I + 2 of II and typical EEG*

OR

1.2.2 I + 2 of II and typical MRI brain scan**

OR

1.2.3 I + 2 of II and positive 14-3-3

OR

1.2.4 Progressive neurological syndrome and positive RT-QuIC in CSF or other tissues

I	Rapidly progressive cognitive impairment
II	A Myoclonus
	B Visual or cerebellar problems
	C Pyramidal or extrapyramidal features
	D Akinetic mutism
III	Typical EEG
IV	High signal in caudate/putamen on MRI brain scan

1.3 **POSSIBLE:**

I + 2 of II + duration < 2 years

* Generalised periodic complexes

** High signal in caudate/putamen on MRI brain scan or at least two cortical regions (temporal, parietal, occipital) either on DWI or FLAIR

2. ACCIDENTALLY TRANSMITTED TSE

2.1 **DEFINITE**

Definite CJD with a recognised iatrogenic risk factor (see box)

2.2 **PROBABLE**

2.2.1 Progressive predominant cerebellar syndrome in human pituitary hormone recipients

2.2.2 Probable CJD with recognised iatrogenic risk factor (see box)

RELEVANT EXPOSURE RISKS FOR THE CLASSIFICATION AS IATROGENIC CJD

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

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

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

3. GENETIC TSE

3.1 **DEFINITE**

3.1.1 Definite TSE + definite or probable TSE in 1st degree relative

3.1.2 Definite TSE with a pathogenic PRNP mutation (see box)

3.2 **PROBABLE**

3.2.1 Progressive neuropsychiatric disorder + definite or probable TSE in 1st degree relative

3.2.2 Progressive neuropsychiatric disorder + pathogenic PRNP mutation (see box)

- **PRNP MUTATIONS ASSOCIATED WITH GSS NEUROPATHOLOGICAL PHENOTYPE**
  P102L, P105L, A117V, G131V, F198S, D202N, Q212P, Q217R, M232T, 192 bpi
- **PRNP MUTATIONS ASSOCIATED WITH CJD NEUROPATHOLOGICAL PHENOTYPE**
  D178N-129V, V180I, V180I+M232R, T183A, T188A, E196K, E200K, V203I, R208H, V210I, E211Q, M232R, 96 bpi, 120 bpi, 144 bpi, 168 bpi, 48 bp*del*
- **PRNP MUTATIONS ASSOCIATED WITH FFI NEUROPATHOLOGICAL PHENOTYPE** D178N-129M
- **PRNP MUTATION ASSOCIATED WITH VASCULAR PRP AMYLOID**
  Y145s
- **PRNP MUTATIONS ASSOCIATED WITH PROVEN BUT UNCLASSIFIED PRION DISEASE**
  H187R, 216 bpi,
- **MUTATIONS ASSOCIATED WITH NEURO-PSYCHIATRIC DISORDER BUT NOT PROVEN PRION DISEASE**
  I138M, G142S, Q160S, T188K, M232R, 24 bpi, 48 bpi, 48 bpi + nucleotide substitution in other octapeptides

ADDITIONAL LIST OF MUTATIONS

• PRNP MUTATIONS WITHOUT CLINICAL AND NEUROPATHOLOGICAL DATA	T188R, P238S
• PRNP POLYMORPHISMS WITH ESTABLISHED INFLUENCE ON PHENOTYPE	M129V
• PRNP POLYMORPHISMS WITH SUGGESTED INFLUENCE ON PHENOTYPE	N171S, E219K, 24 bp deletion
• PRNP POLYMORPHISMS WITHOUT ESTABLISHED INFLUENCE ON PHENOTYPE	P68P, A117A, G124G, V161V, N173N, H177H, T188T, D202D, Q212Q, R228R, S230S

4. vCJD

4.1 **DEFINITE**
1A **and** neuropathological confirmation of vCJD[e].

4.2 **PROBABLE**
4.2.1 I **and** 4/5 of II **and** IIIA **and** IIIB
4.2.2 I **and** IV A[d]

4.3 **POSSIBLE**
I **and** 4/5 of II **and** III A

I	A	Progressive neuropsychiatric disorder
	B	Duration of illness > 6 months
	C	Routine invesitgations do not suggest an alternative diagnosis
	D	No history of potential iatrogenic exposure
	E	No evidence of a familial form of TSE
II	A	Early psychiatric symptoms[a]
	B	Persistent painful sensory symptoms[b]
	C	Ataxia
	D	Myoclonus or chorea or dystonia
	E	Dementia
III	A	EEG does not show the typical appearance of sporadic CJD[c] in the early stages of illness
	B	Bilateral pulvinar high signal on MRI scan
IV	A	Positive tonsil biopsy[d]

a depression, anxiety, apathy, withdrawal, delusions.
b this includes both frank pain and/or dysaesthesia.
c the typical appearance of the EEG in sporadic CJD consists of generalised triphasic periodic complexes at approximately one per second. These may occasionally be seen in the late stages of variant CJD.
d tonsil biopsy is **not** recommended routinely, nor in cases with EEG appearances typical of sporadic CJD, but may be useful in suspect cases in which the clinical features are compatible with vCJD and MRI does not show bilateral pulvinar high signal.
e spongiform change and extensive PrP deposition with florid plaques throughout the cerebrum and cerebellum.

APPENDIX 3

CHANGE IN CLASSIFICATION **IDNO:**

Please enter any changes in classification as they occur

	Classification	Criteria for classification*	Date of change	Reason**
NOTIFICATION				
Between notification and being seen in life				
SEEN IN LIFE				
Life after having been seen				
HIGHEST IN LIFE				
DEATH (including post- mortem result, if performed)				

* 1= Sporadic CJD diagnostic criteria I (Oxford, ***?date***)
2= Sporadic CJD diagnostic criteria II (Rome,1993)
3= Sporadic CJD diagnostic criteria III (Rotterdam, 1998)
4= Variant CJD diagnostic criteria I (CJDSU) - clinical features and neuropathology
5= Variant CJD diagnostic criteria II (UK, 2000) - MRI
6= Variant CJD diagnostic criteria III (UK, 2001) - tonsil bx
7= Sporadic CJD diagnostic criteria IV (Rotterdam, 2010)
8= Sporadic CJD diagnostic criteria V (2017)

** 1= clinical feature (please specify)
2= EEG result
3= MRI result
4= CSF result
5= Brain biopsy result
6= Other
8= RT-QuIC

APPENDIX 4

Professor Richard Knight, Consultant Neurologist (Director NCJDRSU)
Professor R G Will, Consultant Neurologist
Dr Anna Molesworth, Senior Epidemiologist
Elaine Lord, Surveillance Administration Manager
Telephone: 0131 537 2128/1980
Fax: 0131 343 1404

National Creutzfeldt-Jakob
Disease Research & Surveillance Unit
Bryan Matthews Building
Western General Hospital
Crewe Road
EDINBURGH
EH4 2XU

CONSENT FORM

Surveillance of Creutzfeldt-Jakob Disease (CJD)

Please initial box

I have read and understood the relative information sheet for the surveillance of CJD and have had the opportunity to ask questions. I understand that my participation is voluntary and that I am free to withdraw at any time, without my relative's medical care being affected. ☐

I agree to be interviewed regarding, _____ (name), who is my _____ (degree of relative) and to provide information about my relative's past medical and lifestyle history. ☐

I agree for my relative's medical records to be accessed by the surveillance team. ☐

I agree for my relative's dental records to be accessed by the surveillance team. ☐

Name of person giving consent	Signature	Date
Name of person taking consent	Signature	Date

National Creutzfeldt-Jakob Disease
Research & Surveillance Unit,
Western General Hospital,
Edinburgh, EH4 2XU

Surveillance of Creutzfeldt-Jakob Disease (CJD): Relative Information Sheet

You are being invited to contribute to the UK national surveillance of CJD. Before you decide whether or not to take part, it is important for you to understand why surveillance is being done and what it will involve. Please take time to read the following information carefully and ask us if there is anything that is not clear or if you would like more information.

Who is organising the surveillance?

The UK National CJD Research & Surveillance Unit (NCJDRSU) is responsible for CJD surveillance in the UK and research into prion disease and related problems. Surveillance is funded by the Department of Health Policy Research Programme and by the Scottish Government Health Department. The NCJDRSU also receives research funding from these and other individual, charitable, national and international sources.

Why is surveillance undertaken?

CJD is a very rare disease affecting the brain and nervous system. It is one of a group of diseases called prion diseases that exist in different forms. Most cases of CJD have no known cause. However some cases may result from person to person spread via blood transfusion or treatment with certain plasma or hormone products, or certain types of surgery.

The primary aim of CJD surveillance in the UK is to identify changes in the epidemiology of CJD in order to plan for and reduce the potential consequences of this disease and protect public health. As part of this we monitor the characteristics of all forms of CJD, to identify trends in incidence rates and to investigate potential risk factors for the development of disease. We also work closely with the UK Health Departments, the National Blood Authorities, Public Health England (PHE) and Health Protection Scotland (HPS), as well as local public health teams, to provide advice where needed and to help prevent any possible spread of CJD between people.

How can I help?

We would like to use information about your relative's lifestyle, as well as medical and dental histories, for the UK national surveillance of CJD.

If you agree to take part we will ask you questions about your relative, the answers to which we will record on a questionnaire form. The questions relate to your relative's current illness, their past medical and dental history, and their lifestyle - including where they have lived and worked, now and in the past, as well as

their occupation, education, social and recreational history. These questions are fixed and do not alter from one individual to the next. There are no right or wrong answers - we ask for true and accurate answers to the best of the person's knowledge.

After our visit, we also read and take copies of your relative's medical and dental notes to get as complete and detailed a picture as possible of your relative's past history.

Our visit will normally take about two to three hours, although there may be some variation from person to person. During this time you will have the opportunity discuss any aspects of your relative's illness, to discuss the questionnaire and raise any further questions you may have.

Do I have to take part?

No. Participation is voluntary and it is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw your consent at any time with no obligation to explain why. This will not affect the medical care given to your relative.

What are the possible disadvantages and risks of taking part?

We understand that this can be a very stressful time. Thinking and talking about your relative in relation to this research can be distressing. We will do our best to address any issues that worry you.

What are the possible benefits of taking part?

Review by our doctors may help your relative's medical team in supporting a potential diagnosis, or suggesting if CJD seems less likely. In addition, you will be helping us monitor and better understand the causes of CJD in order to plan for and reduce the potential consequences and help protect public health.

Will my taking part in the study be kept confidential?

Yes. All the information we collect during the course of surveillance will be kept confidential and there are strict laws which safeguard your privacy at every stage. All copies of the questionnaire when completed will be kept locked up. Information about your relative will also be kept in a secure database at NCJDRSU. The information will be shared in confidence with your relative's clinicians, GP and public health professionals in order to prevent any possible spread of CJD between people, but at no point in time will your own or your relative's identity be disclosed to anybody outside this investigation team.

What will happen to the results of the study?

We publish regular surveillance updates on our website and in journals, details of which are available at www.cjd.ed.ac.uk. You and your relative will not be identifiable in any published results.

If you have a concern about any aspect of this study or have any further questions we will do our best to answer your questions. Please visit our website www.cjd.ed.ac.uk or contact us at the Unit by calling 0131 537 2128/1980 or email jan.mackenzie@ed.ac.uk.

Thank you for taking the time to read this information sheet.

APPENDIX 5

CLINICAL AND EPIDEMIOLOGICAL REVIEW

SECTION 1
GENERAL INFORMATION

1. IDENTIFICATION INFORMATION

ID Number: | | | | | |

1.1 What is *subject's* name?

First name: _____

Surname: _____

Other name(s): _____

(if subject is female and is/has been married)
record *subject's* maiden name or previous married names if different from current surname

_____

1.2 Sex of *subject?* ☐ 1=male 2=female

1.3 When was *subject* born? ____/____/_____ (dd/mm/yyyy)

1.4 What do you consider to be *subject's* ethnic origin? ☐

1=Caucasian 4=Afro-Caribbean
2=North African 5=Asian
3=Other African 6=Other

1.5 What is *subject's* marital status? ☐

1=single 4=divorced
2=married 5=separated
3=widowed 6=cohabitating

1.6 What is *subject's* present home address?
(*if subject is deceased)* What was *subject's* last home address before s(he) became ill?

House and street: _____

Town: _____

County: _____

Postcode: _____

1.7 Name of *subject's* consultant: _____

1.8 Hospital address

Name of hospital: _____

Street: _____

Town: _____

Postcode: _____

Tel. number: _____

1.9 *Subject's* hospital record number: _____

1.10 *Subject's* NHS number: _____

1.11 Name of *subject's* GP

Name/Practice: _____

Street: _____

Town: _____

Postcode: _____

Tel. number: _____

1.12 Name of *subject's* dentist

Name/Practice: _____

Street: _____

Town: _____

Postcode: _____

Tel No: _____

1.13 Date of interview/examination: ____/____/_____ (dd/mm/yyyy)

1.14 Interview/examination performed by: _____

_____

1.15 What is your (*respondent's)* name?

First name _____

Surname _____

Other names(s) _____

1.16 What is your *(respondent's)* relationship to subject? ☐

1=partner
2=son/daughter
3=nephew/niece
4=sibling
5=cousin
6=father/mother
7=subject themselves
8=other

If other, *specify:*_____

1.17 How long have you know *subject*? ☐☐☐☐
(record year since which *subject* known)

1.18 What is your *(respondent's)* address?

House and street _____

Town _____

County _____

Postcode _____

Telephone _____

1.19 Place of interview: ☐

1=hospital
2=home
3=other

SECTION 2
CLINICAL SURVEILLANCE AND EPIDEMIOLOGICAL REVIEW

BACKGROUND HISTORY

2.1 Surgical History

Surgical history questions refer to *subject's* history **BOTH BEFORE AND AFTER ONSET OF ILLNESS**

Has *subject* ever had any operations, including eye operations or stitching of wounds? ☐ 1= yes 2= not to respondent's knowledge

(If yes), record the year, hospital and type of operation:

1.	Year: _____	Accuracy code (filled in at data entry stage) ☐
	Name of Hospital: _____	
	Operation: _____	Group Category ☐
2.	Year: _____	Accuracy code (filled in at data entry stage) ☐
	Name of Hospital: _____	
	Operation: _____	Group Category ☐
3.	Year: _____	Accuracy code (filled in at data entry stage) ☐
	Name of Hospital: _____	
	Operation: _____	Group Category ☐
4.	Year: _____	Accuracy code (filled in at data entry stage) ☐
	Name of Hospital: _____	
	Operation: _____	Group Category ☐
5.	Year: _____	Accuracy code (filled in at data entry stage) ☐
	Name of Hospital: _____	
	Operation: _____	Group Category ☐
6.	Year: _____	Accuracy code (filled in at data entry stage) ☐
	Name of Hospital: _____	
	Operation: _____	Group Category ☐

7.	Year: _____ Name of Hospital: _____ Operation: _____	Accuracy code (filled in at data entry stage) ☐ Group Category ☐
8.	Year: _____ Name of Hospital: _____ Operation: _____	Accuracy code (filled in at data entry stage) ☐ Group Category ☐
9.	Year: _____ Name of Hospital: _____ Operation: _____	Accuracy code (filled in at data entry stage) ☐ Group Category ☐
10.	Year: _____ Name of Hospital: _____ Operation: _____	Accuracy code (filled in at data entry stage) ☐ Group Category ☐
11.	Year: _____ Name of Hospital: _____ Operation: _____	Accuracy code (filled in at data entry stage) ☐ Group Category ☐
12.	Year: _____ Name of Hospital: _____ Operation: _____	Accuracy code (filled in at data entry stage) ☐ Group Category ☐
	Record the total number of operations ☐☐ 88=not applicable	Total no.of fracture operations ☐☐ (88=N/A 99=N/K)

2.2 Organ or Tissue Transplant

Has *subject* ever received an organ or tissue transplant, including corneal or bone marrow transplant? ☐ 1=yes 2=not to respondent's knowledge

(If yes), record year hospital and organ/tissue(s) received:

Hospital _____ Organ: _____

Hospital _____ Organ: _____

	1=yes 2=not to respondent's knowledge	If yes, record year If no, record 8888
Cornea	☐	☐☐☐☐
Bone Marrow	☐	☐☐☐☐
Kidney	☐	☐☐☐☐
Liver	☐	☐☐☐☐
Other	☐	☐☐☐☐

2.3 Previous Medical History

All further questions in this section refer to *subject's* history **PRIOR TO THE ONSET** of the current illness

Does the *subject* have a record of previous hospital admissions EXCLUDING surgery AND unrelated to the present illness? ☐ 1= yes 2= not to respondent's knowledge

(If yes,) on how many occasions has the *subject* been admitted to hospital (excluding surgery)? ☐☐ 88=not applicable

(If yes), record the hospital name, the date(s) of admission and the reason(s) for admission:

Hospital: _____

Date of Admission: _____

Reason: _____

Hospital: _____

Date of Admission: _____

Reason: _____

Hospital: _____

Date of Admission: _____

Reason: _____

Hospital: _____

Date of Admission: _____

Reason: _____

Hospital: _____

Date of Admission: _____

Reason: _____

Hospital: _____

Date of Admission: _____

Reason: _____

☐☐ Total no.of fracture admissions (non-surgical) 88=N/A 99=N/K)

2.4 Dental History

Since the beginning of 1980 has *subject* had dental treatment? ☐

1=yes
2=not to respondent's knowledge
6=yes, fillings only

(If yes), record a description of the treatment(s) with date(s):

Treatment: _____ Date: _____

Treatment: _____ Date: _____

Treatment: _____ Date: _____

Treatment: _____ Date: _____

Treatment: _____ Date: _____

Treatment: _____ Date: _____

2.5 Blood transfusion

Has *subject* ever received a blood transfusion (blood components or plasma products)?
For suspect cases do not include any transfusions related to current illness

If yes, give year, hospital and reason: ☐

1=yes
2=not to respondent's knowledge

Year: _____

Hospital: _____

Reason _____

2.5 Blood transfusion (cont'd)

Year: _____

Hospital: _____

Reason _____

Year: _____

Hospital: _____

Reason _____

Has *subject* ever received a transfusion of albumin or immunoglobulin?
For suspect cases do not include any transfusions related to current illness

If yes, give year, hospital and reason: ☐ 1=yes 2=not to respondent's knowledge

Year: _____

Hospital: _____

Reason _____

Year: _____

Hospital: _____

Reason _____

Year: _____

Hospital: _____

Reason _____

2.6 **Blood Donation**

Has *subject* ever been a blood donor? ☐ 1=yes 2=not to respondent's knowledge

If yes, date(s) and place(s):

_____

_____

2.7 Has *subject* ever been diagnosed with diabetes or bowel disease? ☐ 1=yes 2=not to respondent's knowledge
(If yes, please give details)

_____

_____

☐ 1=inflammatory bowel disease; 2=insulin-dependant diabetes; 3=other; 4=other bowel disease; 8=not applicable

2.8 Has *subject* ever been to see a psychiatrist?
For suspect cases (and hospital controls) do not include consultations relating to current illness

(If yes, record year, name of psychiatrist, reason and treatment) ☐ 1=yes 2=not to respondent's knowledge

Year: _____

Psychiatrist: _____

Reason: _____

Treatment: _____

Year: _____

Psychiatrist: _____

Reason: _____

Treatment: _____

Year: _____

Psychiatrist: _____

Reason: _____

Treatment: _____

2.9 Course of Injections

Has *subject* ever received a treatment involving a course of injections, for example, human growth hormone, human gonadotrophin, insulin, fertility treatment?
For suspect cases and controls do not include treatments related to current illness

(If yes), record year, name of therapy, frequency and reason): ☐ 1=yes 2=not to respondent's knowledge

Year: _____

Therapy: _____

Frequency: _____

Reason: _____

2.9 Course of Injections (continued)

Year: _____

Therapy: _____

Frequency: _____

Reason: _____

Year: _____

Therapy: _____

Frequency: _____

Reason: _____

Year: _____

Therapy: _____

Frequency: _____

Reason: _____

2.10 Vaccinations

Since beginning of 1980, has *subject* been vaccinated? ☐ 1=yes 2=not to respondent's knowledge

Year: _____

Vaccine: _____

Route: _____

Year: _____

Vaccine: _____

Route: _____

Year: _____

Vaccine: _____

Route: _____

Year: _____

Vaccine: _____

Route: _____

2.11 Procedures involving skin puncture

Has *subject* ever been tattooed? ☐ 1=yes 2=not to respondent's knowledge

Has *subject* ever undergone ear or body piercing? ☐

2.12 Family history

Pedigree (indicating years of birth and death)

Subject's **grandparents**
(including names and dates of birth)

Subject's **parents** and **parents' siblings**
(including names and dates of birth)

Subject and **siblings**
(including names and dates of birth)

Subject's children
(including names and dates of birth)

2.13 Family History

Have any of the blood relatives of the *subject* included in the pedigree above died with dementia (or remain alive with dementia)?

☐ 1=yes
2=not to respondent's knowledge
3=respondent unsure

Have any of these individuals been diagnosed as having Creutzfeldt-Jakob disease?

☐ 1=yes
2=not to respondent's knowledge
3=respondent unsure

(If yes), record the person's name and the approximate date of illness:

Name: _____

Date of illness: _____

Confirmation of family history of CJD from surveillance database

☐ 1=definite case 4=unable to confirm
2=probable case 5=not a case
3=possible case 8=not applicable

2.14 Social Contact

Has *subject* had social contact, through family, friends or work, with someone else who developed CJD?

☐ 1=yes
2=not to respondent's knowledge
3=respondent unsure

(If yes), record the person's name and the approximate date of illness:

Name: _____

Date of illness: _____

Confirmation of social contact with case of CJD from surveillance database

☐ 1=definite case 4=unable to confirm
2=probable case 5=not a case
3=possible case 8=not applicable

Dietary History

1=yes; 2=not to respondent's knowledge

2.15 Has *subject* ever been a vegetarian for a period of one year or more? ☐

(If yes), during what period(s) was *subject* vegetarian, and did s(he) eat any meat or fish at all during this time?

_____

_____

_____

_____

2.16 Additional dietary questions for *subjects* born in or after 1983

Did *subject* ever eat commercially prepared infant/ toddler foods containing **meat** as a young child? ☐

1=yes
2=not to respondent's knowledge
3=respondent unsure
8=not applicable

If yes,

At what age did *subject* **start** eating commercially prepared infant/toddler foods containing **meat?** ☐☐

specify age in months, 88 if not applicable

At what age did *subject* **stop** eating commercially prepared infant/toddler foods containing **meat?** ☐☐

Which brand(s) of commercially prepared infant/toddler foods containing **meat** did the *subject* eat? *If yes,* how often?

	1=yes 2=no 3=respondent unsure 8=not applicable	**Frequency** For frequency, ask respondent to indicate the most appropriate response from those shown on the flash card	
Heinz	☐	☐	
Olvarit	☐	☐	
Cow and Gate	☐	☐	
Milupa	☐	☐	
Farley's	☐	☐	
HiPP Organic	☐	☐	
Baby Organix	☐	☐	
Own brand	☐	☐	If own brand, please indicate which _____
Other	☐	☐	If other brand, please indicate which _____

Did *subject* ever eat commercially prepared infant/toddler foods containing **beef?** ☐

1=yes
2=not to respondent's knowledge
3=respondent unsure
8=not applicable

If no,

Were commercially prepared infant/toddler foods containing **beef** specifically avoided? ☐

2.17 RESIDENTIAL HISTORY (begin with the most recent and work backwards)

	From (dd/mm/yyyy)	To (dd/mm/yyyy)	Street Town County	Postcode	OS grid reference
1	/ /	/ /			E N
2	/ /	/ /			E N
3	/ /	/ /			E N
4	/ /	/ /			E N
5	/ /	/ /			E N
6	/ /	/ /			E N
7	/ /	/ /			E N
8	/ /	/ /			E N
9	/ /	/ /			E N
10	/ /	/ /			E N

2.17 RESIDENTIAL HISTORY (continued)

	From (dd/mm/yyyy)	To (dd/mm/yyyy)	Street Town County	Postcode	OS grid reference
11	/ /	/ /			E N
12	/ /	/ /			E N
13	/ /	/ /			E N
14	/ /	/ /			E N
15	/ /	/ /			E N
16	/ /	/ /			E N
17	/ /	/ /			E N
18	/ /	/ /			E N
19	/ /	/ /			E N
20	/ /	/ /			E N

2.18 OCCUPATIONAL HISTORY OF SUBJECT (begin with the most recent occupation and work backwards)

	From (dd/mm/yyyy)	To (dd/mm/yyyy)	Name of employer	Town	Description of work
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					

2.19 **Summary coding of *subject's* occupational data**

	1=ever 2=never	Number of years elapsed from last work to onset (88=not applicable)
medical/paramedical/nursing/dentistry	☐	☐☐
animal laboratories	☐	☐☐
pharmaceutical laboratories	☐	☐☐
other research laboratories	☐	☐☐
animal farming/veterinary medicine	☐	☐☐
meat industry (butcher's/abbattoirs/rendering plants etc)	☐	☐☐
catering industry	☐	☐☐
other occupational involving animal products (eg leather worker)	☐	☐☐

2.20 **Exposure to animals**

Since the beginning of 1980, has *subject* worked or lived or stayed for more than one week on a farm? ☐

1=lived or worked
2=stayed
3=not to respondent's knowledge

(If lived, worked or stayed), which type of farm was it? ☐

1=arable
2=livestock
3=mixed arable and livestock
4=other
8=not applicable

Duration of stay? _____

2.21 **Education**

How many years of full time education did *subject* complete? ☐☐

(including school, college and university)

2.22 EDUCATIONAL HISTORY OF SUBJECT

(full time education for *subject's* aged less than 50; begin with most recent university/college/school and work backwards

	From (dd/mm/yyyy)	To (dd/mm/yyyy)	Name of Institution Town County	Postcode	OS grid reference
1	/ /	/ /			E N
2	/ /	/ /			E N
3	/ /	/ /			E N
4	/ /	/ /			E N
5	/ /	/ /			E N
6	/ /	/ /			E N
7	/ /	/ /			E N
8	/ /	/ /			E N
9	/ /	/ /			E N
10	/ /	/ /			E N

SECTION 3
EXAMINATION REVIEW

	Examination from notes State of *subject* at admission/first examination by a neurologist
3.1	General Appearance:
3.2	Mental state/speech function:
3.3	Cranial nerves:
3.4	Motor system: Involuntary movements:
3.5	Sensory system:
3.6	Reflexes: primitive: tendon: plantar:
3.7	Cerebellar function/co-ordination

3.8	**NCJDSU Clinician – Examination of the *subject*** General Appearance: bed bound NG/PEG catheterised akinetic mute posture myoclonus startle other involuntary movements
3.9	Mental state/speech functions: best motor response best verbal response eye opening
3.10	Cranial nerves: fields/response to menace pupils EOMs/Doll's eyes
3.11	Motor system: tone power wasting
3.12	Sensory system

3.13	Reflexes primitive: grasp palmomental pout rooting tendon (incl. jaw jerk): plantar:
3.14	Cerebellar function/co-ordination:
3.15	General examination:

3.16 Detailed history of present illness:

CLINICAL HISTORY

3.17 Note the source of information eg hospital notes, relatives, other.

hospital notes ☐
relatives ☐
other ☐

1=yes
2=no
9=not known

If other, specify: _____

3.18 What were the first symptoms of illness noted by the *subject* or their family?

_____

3.19 When did these symptoms first occur? _____ (dd/mm/yyyy)

3.20 When did the *subject* seek medical attention for the illness? _____ (dd/mm/yyyy)

3.21 When was the *subject* first referred to a neurologist? _____ (dd/mm/yyyy)

3.22 When was the *subject* seen by a neurologist? _____ (dd/mm/yyyy)

3.23 When was the *subject* first admitted for the current illness? _____ (dd/mm/yyyy)

3.24 Since the start of the illness, has the *subject* been seen by a psychiatrist? ☐

1=yes
2=no

3.25 If yes, record date of the first consultation: _____ (dd/mm/yyyy)

3.26 SPECIFIC ILLNESS DETAILS Since the start of the illness, until the current time, has the *subject* exhibited the following neurological symptoms/signs:

Symptoms:		**1=Yes 2=No 8=NK 9=Missing**	**Date appeared (dd/mm/yyyy)**	**Signs:**	**1=Yes 2=No 8=NK 9=Missing**	**Date appeared (dd/mm/yyyy)**
Forgetfulness/ memory impairment				Cognitive impairment		
Other higher function impairment				Agnosia		
				Apraxia		
				Visuospatial impairment		
Language disturbance				Dysphasia		
				Dyslexia		
				Dysgraphia		
Psychiatric symptoms				Grasp reflex		
Depression						
Anxiety						
Behavioural disturbance						
Apathy/withdrawal						
Delusions						
Hallucinations	Visual					
	Auditory					
Other psychiatric symptoms						
Disturbance of gait				Cerebellar gait ataxia		
				Spastic		
				Lower motor neurone		
				Other, specify		
Bedbound				Akinetic mutism		
Speech disturbance				Dysarthria		
Visual symptoms	Diplopia			Ocular motor palsy		
	Visual impairment			Hemianopia		
				Cortical blindness		
Weakness or clumsiness of limbs				Pyramidal weakness		
				Extrapyramidal signs		
				Cerebellar signs/nystagmus		
				Lower motor neurone		

Symptoms:		1=Yes 2=No 8=NK 9=Missing	Date appeared (dd/mm/yyyy)	Signs:	1=Yes 2=No 8=NK 9=Missing	Date appeared (dd/mm/yyyy)
Increased limb tone				Rigidity		
				Spasticity		
				Gegenhalten		
				Hyperreflexia		
				Extensor plantar responses		
				Muscle wasting		
				Fasciculation		
				Hypo- or Areflexia		
Involuntary movements				Myoclonus		
				Chorea		
				Dystonia		
				Other, specify		
Sensory symptoms	Numbness/tingling/ paraesthesia				1=yes 2=no 3=central origin 4=peripheral origin 9=uncertain	Date appeared dd/mm/yyyy
	Pain /burning / discomfort			Sensory signs		
Seizures						

3.27 TREATMENT

Specify drug therapy for TSE ☐

0=No treatment
1=Quinacrine
2=Oral PPS
3=Intra-ventricular PPS
4=Tetracycline (doxycycline)
5=Other, specify: _____

Complications of surgery ☐

Complications of intra-ventricular catheter ☐

Complications of pump ☐

1=yes
2=no
9=missing

Significant drug side effects ☐

1=yes, withdrawal of drugs
2=yes, decrease of therapeutic dose
3=yes, but no change of the therapeutic dose
4=no
9=missing

Significant evidence of benefit ☐

1=clinical improvement
2=EEG improvement
3=MRI improvement
4=14-3-3 improvement
5=other improvement
6=no
8=Other, specify _____
9=missing

SECTION 4
REVIEW OF INVESTIGATIONS

INVESTIGATIONS

4.1 EEG

Has the *subject* undergone an EEG? ☐ 1=yes; 2=no; 9=not known

(If yes), on how many occasions? ☐☐

(If yes), record date of most recent EEG ____/____/_____(dd/mm/yyyy)

Are EEG records/copies available in the Unit ☐ 1=yes; 2=yes,some; 3=no; 8=not applicable

Have the EEGs been examined by a Unit staff member? ☐ 1=yes; 2=no; 8=not applicable

Has the patient recorded an EEG characteristic of CJD (generalised triphasic periodic complexes with frequency about 1/s) ☐
1=yes, confirmed by Unit staff
2=yes, reported by local staff, EEG not available for confirmation by Unit staff
3=no
8=no EEG performed

(If yes), record the date on which the first characteristic EEG was recorded ____/____/_____ (dd/mm/yyyy)

4.2 CT Scan

Has the *subject* ever had a CT scan? ☐ 1=yes; 2=no; 9=not known

Has the patient ever had an abnormal CT scan? ☐
1=yes, confirmed by Unit staff
2=yes, reported by local staff, scan not available for confirmation by Unit staff
3=no
8=no scan performed

(If yes), record the date on which the first abnormal scan was performed? ____/____/_____ (dd/mm/yyyy)

(If yes), specify what abnormalities have been observed _____

_____

_____

4.3 MRI Scan

Has the *subject* ever had an MRI scan? ☐ 1=yes; 2=no; 9=not known

(If yes), on how many occasions? ☐☐

(If yes), record date of most recent scan _____/_____/_____(dd/mm/yyyy)

Are MRI scans available in the Unit ☐ 1=yes 2=yes,some 3=no 8=not applicable

Have the MRI scans been examined by a Unit staff member? ☐

Has the patient ever had an abnormal MRI scan? ☐ 1=yes, confirmed by Unit staff 2=yes, reported by local staff, scan not available for confirmation by Unit staff 3=no 8=no scan performed

(If yes), record the date on which the first abnormal scan was performed? _____/_____/_____ (dd/mm/yyyy)

(If yes), specify what abnormalities have been observed _____

_____

_____

(If an abnormal MRI scan has been reported by someone outside the unit) who reported the abnormal scan?

Name: _____

Address _____

_____

_____

4.4 **CSF findings** (fill coding boxes with 8s if test results are not available)

Date of first CSF collection ____/____/_____ (dd/mm/yyyy)

Results:

protein	☐☐.☐☐ g/l
CSF glucose / serum glucose	☐☐/☐☐ . ☐☐ mmol/l
WBC / RCC	☐☐☐☐ / ☐☐☐☐ count/mm³
14-3-3	☐ 1=negative 2=equivocal 3=positive
NSE	☐☐☐.☐ ng/ml
S100b	☐☐.☐☐ ng/ml
tau	☐☐☐☐☐ pg/ml

Ig oligoclonal bands in:

CSF	☐ 1=positive, 2=negative
blood	☐ 1=positive, 2=negative

Date of second CSF collection ____/____/_____ (dd/mm/yyyy)

Results:

protein	☐☐.☐☐ g/l
CSF glucose / serum glucose	☐☐/☐☐ . ☐☐ mmol/l
WBC / RCC	☐☐☐☐ / ☐☐☐☐ count/mm³
14-3-3	☐ 1=negative 2=equivocal 3=positive
NSE	☐☐☐.☐ ng/ml
S100b	☐☐.☐☐ ng/ml
tau	☐☐☐☐☐ pg/ml

Ig oligoclonal bands in:

CSF	☐ 1=positive, 2=negative
blood	☐ 1=positive, 2=negative

4.5 Has the *subject* had neurophysiology studies done? ☐ 1=yes 2=no 9=not known

4.6 Has the *subject* had any abnormalities on other routine biological/haematological investigations during this illness? ☐ 1=yes 2=no 9=not known

(If yes), describe the investigation(s) and the abnormalities:

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

4.7 Has the *subject* undergone neuropsychological assessment? ☐ 1=yes 2=no 9=not known

Type of examination? ☐ 1=MMSE 2=Other, specify_____ 3=Formal Neuropsychometry 4= Multiple

Result

Score for MMSE _____

Score from other test (score)

_____

(please specify other test)

Is neuropsychology report available? ☐ 1=yes 2=no 9=not known

4.8 Has the *subject* undergone a brain biopsy? ☐ 1=yes 2=no 9=not known

(If yes), were there any complications? ☐ 1=yes 2=no 9=not known

Result _____

4.9 Has the *subject* undergone a tonsil biopsy? ☐ 1=yes 2=no 9=not known

(If yes), were there any complications? ☐ 1=yes 2=no 9=not known

Result _____

4.10 Specimens Collected

	1=yes 2=no	Quantity (mls)
Blood: Frozen for general use	☐	☐☐
Separated and frozen	☐	☐☐
Urine	☐	☐☐
CSF	☐	☐☐

4.11 Post Mortem

Date of death: ____/____/_____

Was a post mortem performed? ☐ 1=yes 2=no 9=not known

(If yes), is neuropathological material available? ☐ 1=yes 2=no 8=not applicable 9=not known

(If material is available) is material available in Edinburgh? ☐

Are post mortem results available? ☐ 1=yes 2=no 9=not known

4.12 PrP Genotype

Are PrP genotype data available? ☐ 1=yes 2=no 9=not known

(If yes), what was the *subject's* codon 129 genotype ☐ 1=MM 2=MV 3=VV

(If yes), did the subject carry a mutation? ☐ 1=yes 2=no 8=not done 9=missing

(If mutation), specify: _____

4.13 **Subject Classification**

On the basis of the available information, what is the classification of the *subject*?

☐☐.

1.0=definite CJD
2.0=probable CJD
3.0=possible CJD
4.1=diagnosis unclear
4.2=CJD thought unlikely
4.3=definitely not CJD
5.0=GSS
0.0=unclassified

(If subject is classified as at least possible CJD or GSS) which category of disease is suspected? ☐

S=sporadic CJD
N=variant CJD
F=familial CJD
I=iatrogenic CJD
G=GSS

Presenting symptoms ☐

1=rapidly progressive dementia
2=Heidenhain
3=Pure psychiatric onset
4=progressive dementia
5=pure cerebellar onset
6=stroke-like onset
8=other, specify: _____
9=missing

CODING FOR BABY FOOD FREQUENCIES

Response	Code
never	1
less than once per year	2
about once a year	3
several times per year	4
about once per month	5
about once per week	6
several times per week	7
several times per day	8

APPENDIX 6

BEEF & BEEF PRODUCT PURCHASING QUESTIONS ***NAME*** _____

To be completed for ALL SUSPECT VCJD CASES

Relevant for time period 1980-1996

BUTCHER

Did your relative eat beef burgers, beef mince, sausages, meat pies, steaks or joints of beef bought from a **butcher** between 1980 and 1996? If he/she did, please indicate in the table below **where** they were bought from, over what **time period** and how **frequently** they were **eaten** by your relative.

Name & address of butcher	**Type of establishment- local, regional, national, other (please specify)**	**Over which time period**	**Frequency of consumption**

BEEF & BEEF PRODUCT PURCHASING QUESTIONS ***NAME*** _____
To be completed for ALL SUSPECT VCJD CASES
Relevant for time period 1980-1996

EXAMPLE ONLY

BUTCHER

Did your relative eat beef burgers, beef mince, sausages, meat pies, steaks or joints of beef bought from a **butcher** between 1980 and 1996? If he/she did, please indicate in the table below **where** they were bought from, over what **time period** and how **frequently** they were **eaten** by your relative.

Name & address of butcher	**Type of establishment- local, regional, national, other (please specify)**	**Over which time period**	**Frequency of consumption**
Eg. Blogs & Sons, The High Street, Ten Town	*Local butcher*	*1980-1996*	*Once per week*
Eg. Dinhirst Family Butchers, Eddlecity Branch, Main Street, Eddlecity	*Regional butcher*	*1985-1989*	*Several times a week*

Examples of type of establishment meat was purchased at:

- Local
- Regional
- National
- other (please specify)

Examples of frequency of consumption of meat

- never
- less than once a year
- about once a year
- several times a year
– about once a month
– about once a week
– several times a week
– several times a day

BEEF & BEEF PRODUCT PURCHASING QUESTIONS ***NAME*** _____

To be completed for ALL SUSPECT VCJD CASES

Relevant for time period 1980-1996

CORNER SHOP/ MINIMART

Did your relative eat beef burgers, beef mince, sausages, meat pies, or other ready prepared meals containing beef bought from a **corner shop/ minimart** between 1980 and 1996? If he/she did, please indicate in the table below **where** they were bought from, over what **time perio**d and how **frequently** they were **eaten** by your relative.

Name & address of corner shop/ minimart	**Type of establishment- local, regional, national, other (please specify)**	**Over which time period**	**Frequency of consumption**

BEEF & BEEF PRODUCT PURCHASING QUESTIONS ***NAME*** _____

To be completed for ALL SUSPECT VCJD CASES

Relevant for time period 1980-1996

SUPERMARKET

Did your relative eat beef burgers, beef mince, sausages, steaks or joints of beef, meat pies, or other ready prepared meals containing beef bought from a **supermarket** between 1980 and 1996? If he/she did, please indicate in the table below **where** they were bought from, over what **time period** and how **frequently** they were **eaten** by your relative.

Name & address of supermarket	**Type of establishment- local, regional, national, other (please specify)**	**Over which time period**	**Frequency of consumption**

BEEF & BEEF PRODUCT PURCHASING QUESTIONS ***NAME*** _____
To be completed for ALL SUSPECT VCJD CASES
Relevant for time period 1980-1996

FREEZER CENTRE
Did your relative eat beef burgers, beef mince, sausages, meat pies, steaks or joints of beef bought from a **freezer centre** between 1980 and 1996? If he/she did, please indicate in the table below **where** they were bought from, over what **time period** and how **frequently** they were **eaten** by your relative.

Name & address of freezer centre	**Type of establishment- local, regional, national, other (please specify)**	**Over which time period**	**Frequency of consumption**

BEEF & BEEF PRODUCT PURCHASING QUESTIONS ***NAME*** _____
To be completed for ALL SUSPECT VCJD CASES
Relevant for time period 1980-1996

ABATTOIR, MOBILE VAN, MARKET, FARM SHOP/ GATE

Did your relative buy beef burgers, beef mince, sausages, meat pies, steaks or joints of beef from an **abattoir, mobile van, market or farm shop/ gate** between 1980 and 1996? If he/she did, please indicate in the table below **where** they were bought from, over what **time period** and how **frequently** they were **eaten** by your relative.

Name & address of abattoir, mobile van, market, farm shop/ gate	**Type of establishment- local, regional, national, other (please specify)**	**Over which time period**	**Frequency of consumption**

BEEF & BEEF PRODUCT PURCHASING QUESTIONS ***NAME*** _____

To be completed for ALL SUSPECT VCJD CASES

Relevant for time period 1980-1996

FAST FOOD OUTLETS, PUBS, RESTAURANTS

Did your relative use/eat in fast food outlets, pubs or restaurants regularly between 1980 and 1996? If he/she did, please indicate in the table below **where** the outlet was, **type of food** purchased, over what **time period** and how **frequently** they were **eaten** by your relative.

Name & address of fast food outlet, pub or restaurant	Type of food purchased	Over which time period	Frequency of consumption

GP MEDICAL HISTORY FORM

1. SUBJECT IDENTIFICATION INFORMATION

(to be completed prior to visit) id number

First name: _____

Surname: _____

Date of birth: _____/_____/_____ (dd/mm/yy)

Date of onset: _____/_____/_____ (dd/mm/yy)

Medical notes found (1=yes, 2=no): ☐

If no, leave the rest of the form blank.

In which year do the medical notes available begin? ☐☐☐☐

2. GENERAL PRACTICE IDENTIFICATION INFORMATION

Practice name: _____

_____

Address: _____ Building

_____ Street

_____ Town

_____ Postcode

_____ Phone

Review of GP medical notes performed by:

Review date:

3. PREVIOUS MEDICAL HISTORY

Complete this section of the form using the medical notes available. **For individuals who developed Creutzfeldt-Jakob disease, all questions refer to the patient's history prior to the onset of the disease.**

NON-SURGICAL ADMISSIONS

3.1 Has the person ever been admitted to hospital (excluding surgery AND unrelated to CJD or current admission for hospital control)? ☐ 1=yes 2=no

If **YES**, on how many occasions has the person been admitted to hospital**?** ☐☐ 88=N/A 99=N/K

If **YES**, record the date of admission, name of the hospital, its location (town) and the reason for admission, starting with the most recent admission.

☐☐ Total no.of fracture admissions (non-surgical) 88=N/A 99=N/K)

1. _____
   _____
   _____
2. _____
   _____
   _____
3. _____
   _____
   _____
4. _____
   _____
   _____
5. _____
   _____
   _____

3.1 (continued) If **YES**, please record the date of admission, name of the hospital, its location (town) and the reason for admission, starting with the most recent admission. 6. _____ _____ _____ 7. _____ _____ _____ 8. _____ _____ _____ 9. _____ _____ _____ 10. _____ _____ _____ 11. _____ _____ _____ 12. _____ _____ _____	

3.4

INFLAMMATORY BOWEL DISEASE

3.2 Has the person ever been diagnosed as having inflammatory bowel disease? (1=yes, 2=no) ☐

If **YES**, in which year was this first diagnosed? (8888=not applicable, 9999=unknown) ☐☐☐☐

DIABETES

3.3 Has the person ever been diagnosed as diabetic? (1=yes, 2=no, 8=not applicable) ☐

If **YES**, in which year was the diagnosis first made? (8888=not applicable, 9999=unknown) ☐☐☐☐

If **YES**, has the person ever received insulin? (1=yes, 2=no, 8=not applicable, 9=unknown) ☐

If **YES**, in which years did the person first receive and last receive insulin (8888=N/A, 9999=N/K)? First year ☐☐☐☐

Last year ☐☐☐☐

SURGERY

3.4 Has the person ever undergone surgery, including eye operations involving physical contact or stitching of wounds, (excluding operations related to CJD or current admission for hospital controls)? (1=yes, 2=no) ☐

If **YES**, has the person ever undergone neurosurgery? (1=yes, 2=no, 8=not applicable) ☐

If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed.

No. of neuro-surgical operations ☐☐
88=N/A, 99=N/K

_____

_____

_____

First and last years ☐☐☐☐ ☐☐☐☐
8888=N/A, 9999=N/K

3.5 (surgical history continued)

ABDOMINAL, INCLUDING APPENDECTOMY

If **YES**, has the person ever undergone abdominal/pelvic surgery, including removal of appendix? (1=yes, 2=no, 8=not applicable) ☐

If so, record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed.

_____

_____

_____

_____

_____

_____

_____

_____

_____

GYNAECOLOGICAL

If **YES**, has the person ever undergone gynaecological surgery? (1=yes, 2=no, 8=not applicable) ☐

If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed.

_____

_____

_____

_____

_____

_____

3.4 (surgical history continued)

ORTHOPAEDIC

If **YES**, has the person ever undergone orthopaedic surgery? (1=yes, 2=no, 8=not applicable) ☐

If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed.

_____

_____

_____

_____

_____

_____

_____

EYE

If **YES**, has the person ever undergone eye surgery? (1=yes, 2=no, 8=not applicable) ☐

If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed.

_____

_____

_____

_____

_____

_____

_____

3.4 (surgical history continued)

EAR

If **YES**, has the person ever undergone ear surgery? (1=yes, 2=no, 8=not applicable) ☐

If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed.

_____

_____

_____

_____

_____

_____

CARPAL TUNNEL ☐

If **YES**, has the person ever undergone carpal tunnel surgery? (1=yes, 2=no, 8=not applicable)

If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed.

_____

_____

_____

_____

_____

_____

3.4 (surgical history continued)

DISCS

If **YES**, has the person ever undergone disc surgery? (1=yes, 2=no, 8=not applicable) ☐

If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed.

_____

_____

_____

_____

TONSILLECTOMY

If **YES**, has the person ever undergone tonsillectomy? (1=yes, 2=no, 8=not applicable) ☐

If so please record the year surgery took place and the name and place of the hospital.

_____

_____

TRANSPLANT

If **YES**, has the person ever undergone organ or tissue transplant surgery including corneal or bone marrow transplant? (1=yes, 2=no, 8=not applicable) ☐

If so please record the year(s) transplant took place, the name(s) and place(s) of the hospital, and the organ received.

_____

_____

_____

_____

3.4 (surgical history continued)

OTHER OPERATIONS

If **YES**, has the person ever undergone any other surgical procedure not included in the categories above? (1=yes, 2=no, 8=not applicable) ☐

If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed.

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

3.5 How many times **IN TOTAL** has the person undergone surgery? (88=not applicable) ☐☐

☐☐ Total no.of fracture operations (88=N/A,99=N/K)

BLOOD/BLOOD PRODUCTS

3.6 Has the person ever received a transfusion of blood or blood products such as albumin or immunoglobulin (excluding those received relating to CJD, or relating to current admission for hospital controls? (1=yes, 2=no)

If **YES,** please record the year(s) the transfusion took place, the name(s) and place(s) of the hospital, and the product(s) received.

_____

_____

_____

_____

_____

_____

INJECTION TREATMENT

3.7 Has the person ever received a treatment involving a course of injections, (excluding those related to CJD or current admission for hospital controls)? (1=yes, 2=no)

If **YES**, please record the year(s) of the treatment(s), the medication(s) involved and the reason(s)

_____

_____

_____

_____

_____

_____

_____

_____

Injectable therapy containing bovine derivatives (1=yes, 2=no, 3=unsure, 8=not applicable)

VACCINES

3.8 Since 1980, has the person received any vaccines? (1=yes, 2=no, 3=unsure, 9=unknown) ☐

If **YES**, fill in the following information regarding the vaccine number

Vaccine	Date Given	Batch Number

ALLERGY TESTING

3.9 Has the person ever been tested for allergy (exclude those related to CJD or current admission for hospital controls? (1=yes, 2=no) ☐

If **YES**, please record year and place the testing was performed, and describe the procedures involved.

_____

_____

_____

ACUPUNCTURE

3.10 Has the person ever undergone acupuncture (exclude if related to CJD or current admission for hospital controls)? (1=yes, 2=no) ☐

If **YES**, please record year and where the acupuncture was performed

_____

_____

NON-INJECTABLE TREATMENTS

3.11 Record non-injectable treatments, lasting more than 4 weeks, since 1984. Do not include treatments related to current condition for cases or hospital controls. **Do include**: oral medicines, hormone supplements including oral contraceptives and HRT, topical therapies including eyedrops. **Duration in days, weeks, months or years**. **Year started Duration Drug name Reason**		
1.		
2.		
3.		
4.		
5.		
6.		
7.		
8.		
9.		
10.		
11.		
12.		
13.		
14.		
15.		
16.		
17.		
18.		
19.		
	Non-injectable therapy containing bovine derivatives (1=yes, 2=no, 3=unsu **8=not applicable)**	

PSYCHIATRIST

3.12 Has the person ever been referred to a psychiatrist (excluding any referrals related to Creutzfeldt-Jakob disease or current admission for hospital controls? (1=yes, 2=no)

If **YES**, how many times has the person been referred? ☐☐ 88=N/A 99=N/K

If **YES**, year of first referral: ☐☐☐☐

year of most recent referral: ☐☐☐☐

8888=NA, 9999=NK

If **YES**, please record the year, the name and address of the psychiatrist, and the reason for referral

_____

_____

_____

_____

_____

_____

_____

_____

4. CASES ONLY - surgical and medical history after onset of CJD

Complete this section of the form using the medical notes available. **All questions refer to the patient's history after onset of CJD.**

4.1 Has the person undergone surgery, including eye operations involving physical contact or stitching of wounds, and including minor surgery within the practice after onset of CJD (see onset date on front cover)? (1=yes, 2=no) ☐

If **YES**, has the person undergone neurosurgery (1=yes, 2=no, 8=not applicable). ☐

If so, please record the year(s) the surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed.

_____

_____

_____

_____

_____

If **YES**, has the person undergone abdominal surgery, including removal of appendix? (1=yes, 2=no, 8=not applicable) ☐

If so, record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed.

_____

_____

_____

_____

_____

_____

4.1	If **YES**, has the person undergone orthopaedic surgery? (1=yes, 2=no, 8=not applicable) If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed. _____ _____ _____	☐
	If **YES**, has the person undergone eye surgery? (1=yes, 2=no, 8=not applicable) If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed. _____ _____ _____	☐
	If **YES**, has the person undergone gynaecological surgery? (1=yes, 2=no, 8=not applicable) If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed. _____ _____ _____	☐
	If **YES**, has the person undergone carpal tunnel surgery? (1=yes, 2=no, 8=not applicable) If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed. _____ _____ _____	

4.1 If **YES**, has the person undergone disc surgery? (1=yes, 2=no, 8=not applicable) ☐

If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed.

_____

_____

_____

If **YES**, has the person undergone ear surgery? (1=yes, 2=no, 8=not applicable) ☐

If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed.

_____

_____

_____

If **YES**, has the person undergone tonsillectomy? (1=yes, 2=no, 4=Tonsil Biopsy, 8=not applicable) ☐

If so please record the year surgery took place and the name and place of the hospital.

_____

_____

If **YES**, has the person undergone transplant surgery including corneal or bone marrow transplant? (1=yes, 2=no, 8=not applicable) ☐

If so please record the year(s) transplant took place, the name(s) and place(s) of the hospital, and the organ received.

_____

_____

4.1 If **YES**, has the person undergone any other surgical procedure not included in the categories above? (1=yes, 2=no, 8=not applicable) If so please record the year(s) surgery took place, the name(s) and place(s) of the hospital, and the procedure(s) performed. _____ _____ _____ _____ _____ _____ _____	☐
4.2 How many times **IN TOTAL** has the person undergone surgery since the onset of CJD? (88=not applicable)	☐☐

4.3	Has the person had any **other admissions (i.e. other than "surgery")** to hospital since onset? (1=yes, 2=no, 8=not applicable) Please record date, name of hospital, town of hospital and reason for **medical admissions since the onset of the current illness** excluding those related to operations mentioned above. 1._____ _____ _____ 2._____ _____ _____ 3._____ _____ _____ 4._____ _____ _____ 5._____ _____ _____ 6._____ _____ _____ 7._____ _____ _____	☐

APPENDIX 8

Professor Richard Knight, Director (NCJDRSU) 0131 537 2128
Dr Anna Molesworth, Epidemiologist 0131 537 3091
Elaine Lord, Surveillance Administration Manager 0131 537 3104
Fax: 0131 343 1404

National Creutzfeldt-Jakob
Disease Research & Surveillance Unit
Bryan Matthews Building
Western General Hospital
Crewe Road
EDINBURGH
EH4 2XU

August 2016

To: All Neurologists in the UK

Dear Colleague,

REPORTING CJD CASES AND SUSPECT CASES TO LOCAL PUBLIC HEALTH TEAMS

The National CJD Research & Surveillance Unit (NCJDRSU) is working with public health doctors to prevent any possible spread of CJD between people. This is vital, as patients with CJD may have had surgery, or donated blood or other tissues, and a local response may be required to help prevent spread.

To carry out this important public health action, when you refer cases and suspect cases to us, **PLEASE ALSO INFORM YOUR LOCAL HEALTH PROTECTION/PUBLIC HEALTH TEAM** if you have not already done so. Your Trust's **INFECTION CONTROL TEAM** should also be informed of the case/suspect case; they should be able to identify contact details of the local health protection/public health team if necessary.

Public health doctors should be informed about **all cases/suspect cases of CJD** using the reporting form overleaf. This includes those cases which do not fulfil the surveillance criteria for CJD (see http://www.cjd.ed.ac.uk/documents/criteria.pdf), but where the diagnosis of CJD is being actively considered. The public health doctors will then work with the relevant trusts, hospitals or health boards to investigate and manage any public risk. To support the public health follow-up, the NCJDRSU will inform your local health protection/public health team of the CJD diagnosis and provide your contact details. The local health protection/public health team may then contact you directly if you have not been in contact with them already regarding the case.

All cases of suspect CJD should continue to be notified to the National CJD Research & Surveillance Unit (NCJDRSU) in Edinburgh and the National Prion Clinic (NPC) in London in accordance with the system outlined in the Chief Medical Officer's letter of July 2004.

Many thanks for your help.
Yours sincerely

Professor Richard Knight
Consultant Neurologist
Director (NCJDRSU)

Dr Anna Molesworth
Epidemiologist

PUBLIC HEALTH CJD REPORTING FORM August 2016

To the reporting clinician: please complete the following information for reporting cases and suspect cases of CJD to your local health protection/public health team. They may then use this information to help them follow-up your patient's medical records. The health protection/public health team may contact you for more information if needed.

Name of **reporting clinician** _____

Contact details _____

_____

Name of lead consultant in health protection/public health _____

Contact details _____

_____

Name of patient _____

Date of birth _____

Unique Patient **NCJDRSU Number** _____

Current / last known **address** of patient _____

Name and details of **GP** of patient _____

_____

The patient has been **diagnosed** with	(Please tick)	The **type of CJD** is thought to be	(Please tick)
Possible CJD	☐	Sporadic CJD	☐
Probable CJD	☐	Variant CJD	☐
Definite CJD	☐	Iatrogenic CJD	☐
Other (specify)	☐ ……	Familial CJD or GSS	☐

Onset date ……

The patient has been brought to the attention of **NCJDRSU** Yes ☐ No☐
The patient has been brought to the attention of the **NPC** Yes ☐ No☐

Comment

Signature of reporting doctor…… Date……

To the local health protection/public health team: guidance on the public health actions to be taken following a report of a new case of CJD is available at:
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/474338/CJD_public_health_action_new_case_301015.pdf

APPENDIX 9

CJD Surveillance Unit

CONFIDENTIAL: FOR IMMEDIATE ACTION

Notification of vCJD to UK Blood Transfusion Services TMER No.

Notify by telephone to Medical Directors (see below), followed by written confirmation (secure email). Please retain copy at CJDSU and send anonymised copy (1st class post) to DH as detailed below.

Notified by:		Date notified:		
Surname:		Previous / maiden name(s)		
Forename(s):		Sex: (circle M or F)	M	F
Date of birth:		Putative donor: (circle Yes or No)	Yes	No
Last known address:				
Previous addresses (with dates):				
Donation dates:				
Place(s) of donation (with dates):				
Additional information:				
*Status of vCJD (circle one response)	Strongly Suspected	Confirmed		

Notified to:	Plus anonymised copy (by 1st class post) to:
Medical Director, National Blood Authority Medical Director, Scottish NBTS Medical Director, Welsh BTS Medical Director, N. Ireland BTS	Dr R Jecock, DH Dr C Calderwood, CMO Scottish Government , Welsh Assembly Dr E Mitchell, DHSS (NI)

**Further information required when status changes*

CONFIDENTIAL
TO CJD SURVEILLANCE UNIT

ACKNOWLEDGEMENT OF RECEIPT
OF NOTIFICATION OF vCJD TO UK BLOOD TRANSFUSION SERVICES

FOR THE ATTENTION OF JAN MACKENZIE

Email: janet.mackenzie1@nhs.net

I confirm that notification was received for .....

on ..... and is being acted upon.

Name (print) ..... Date .....

South East Scotland Research Ethics Service

Waverley Gate
2-4 Waterloo Place
Edinburgh
EH1 3EG

NHS Lothian

Name: Jan Mackenzie
Address: National CJD Research
& Surveillance Unit
Western General Hospital
Edinburgh
EH4 2XU
UK

Date: 04/03/2016
Your Ref:
Our Ref: NR/162AB13
Enquiries to: Alex Bailey
Direct Line: 0131 465 5679
Email: alex.bailey@nhslothian.scot.nhs.uk

Dear Jan,

Project Title: Surveillance of CJD in the UK

You have sought advice from the South East Scotland Research Ethics Service on the above project. This has been considered by the Scientific Officer and you are advised that, based on the submitted documentation (email correspondence and NCJDRSU surveillance protocol), it does not need NHS ethical review under the terms of the Governance Arrangements for Research Ethics Committees (A Harmonised Edition).

The advice is based on the following:

- *The project is public health surveillance*

If the project is considered to be health-related research you will require a sponsor and ethical approval as outlined in The Research Governance Framework for Health and Community Care. You may wish to contact your employer or professional body to arrange this. You may also require NHS management permission (R&D approval). You should contact the relevant NHS R&D departments to organise this.

For projects that are not research and will be conducted within the NHS you should contact the relevant local clinical governance team who will inform you of the relevant governance procedures required before the project commences.

This letter should not be interpreted as giving a form of ethical approval or any endorsement of the project, but it may be provided to a journal or other body as evidence that NHS ethical approval is not required. However, if you, your sponsor/funder feel that the project requires ethical review by an NHS REC, please write setting out your reasons and we will be pleased to consider further. You should retain a copy of this letter with your project file as evidence that you have sought advice from the South East Scotland Research Ethics Service.

Yours sincerely,

Alex Bailey
Scientific Officer
South East Scotland Research Ethics Service