Chronology of events and significant announcements on vCJD

Date	Event
25 Nov 87	FDA Office of Biologics Memorandum "*Deferral of donors who have received human pituitary-derived growth hormone*"
13 Mar 95	CPMP/BWP/269/95 "*Note for Guidance on plasma-derived medicinal products*" revised guidance, including donor deferral for individuals treated with human pituitary extracts or with family history of CJD.
20 Mar 96	CEM/CMO/96/1 "Message from Sir Kenneth Calman, Chief Medical Officer" confirming recognition of a new variant of CJD, possibly linked to BSE.
6 Apr 96	Publication of landmark Lancet article "A New Variant of Creutzfeldt-Jakob Disease in the UK" by Bob Will and co-workers
11 Dec 96	FDA CBER Memorandum "*Revised Precautionary Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) by Blood and Blood Products*" – provides the agency's current thinking on donors considered to be CJD risk; requirements on recall and advice to consignees
1 Jul 97	DH (97/153) report advice from SEAC on research into the link between nvCJD and BSE which concluded "*... the most likely explanation for the cases of the new variant CJD was exposure to BSE before the introduction of the Spongiform Bovine Offals (SBO) ban in 1989.*"
Oct 97	Three UK (English) plasma donors confirmed as having died from nvCJD (total number of definite vCJD cases at the time = 22)
30 Oct 97	BPL recall (PR97/205) Factor VIII and albumin from pool with definite vCJD donor (1st)
31 Oct 97	Advice to BPL of 2nd definite vCJD donor (K97/347) – no in-date product, no recall (in this regard note later advice of CPMP/201/98)
Nov 97	BBC Panorama programme, "The British Disease"
4 Nov 97	BPL recall (PR97/208) Factor VIII and albumin from pool with definite vCJD donor (3rd)
5 Nov 97	EMEA statement on vCJD for BBC "Newsnight" (recall inappropriate for classical CJD; position on vCJD under review)
6 Nov 97	SEAC Meeting Public Summary (97/333) confirms advice to DH on safety of blood and blood products in respect of vCJD
6 Nov 97	DH (97\335) accept SEAC advice to commission risk assessment on blood and blood products
18 Nov 97	Recall (by Nycomed Amersham) of Pulmonate II prepared using vCJD-affected BPL albumin
20 Nov 97	CPMP press release (CPMP/1056/97) including a statement on nvCJD and blood products advises "... as a *precautionary measure ... prudent to withdraw batches of plasma derived medicinal products ...donor ... confirmed diagnosis of nvCJD ... consequences for essential medicinal products where alternatives may be unavailable will need careful consideration.*"
25 Nov 97	First CBER notification of product recall (IV IgG, Sandoglobulin) resulting from use of albumin excipient implicated by inclusion of CJD-risk donation
27 Nov 97	UKHCDO press release recommending use of recombinant Factor VIII[i]

Dec 97	UKHCDO statement on preferred concentrates makes UK-derived f.VIII product of last resort
3 Dec 97	UK "Beef on the Bone" ban
11 Dec 97	FDA "Dear Biologic Product Manufacturer" letter, advising manufacturers of CJD-implicated plasma product batches and requiring notification within 30 days of any batch used at any stage during manufacture of a licensed product.
16 Dec 97	NBA/BPL Position Statement on "*the nature of advice to be given to patients who have been treated with plasma products manufactured from a plasma pool which includes plasma from a donor suffering from nvCJD*"
6 Feb 98	PL (CO) (98) 1: DH provided "general" advice on patient notification "New Variant CJD – Patients who have received implicated blood products" – recipients need not be notified – but clinician i/c free to exercise judgement
26 Feb 98	DH (98/076) BPL to be allowed to import plasma; NBA to prepare leucodepletion strategy
26 Feb 98	CEM/CMO/98/5 reports CSM advice: product to be recalled if donor strongly suspected of vCJD; vaccines used in UK don't contain UK albumin
26 Feb 98	CPMP/201/98: no evidence of transmission of classical CJD by blood/plasma; vCJD recognisably different, therefore precautionary recall of plasma products, this to include informing "supply chain" even if products exhausted; excipient albumin not to be sourced from countries with vCJD
Apr 98	France, Ireland and Portugal mandate total leucodepletion
1 Apr 98	BPL and PFC make presentations to a Special Subcommittee of CSM on vCJD risk from products manufactured from UK plasma
5 May 98	Meeting involving DH, Scottish Office, CJDSU, SNBTS and NBA/BPL to review basis and mechanisms of advice of vCJD infection – CJDSU to notify blood services only when vCJD confirmed or "strongly suspected" (i.e. probable)
13 May 98	CSM/98/8th Meeting – considered manufactured blood products should not be sourced from UK plasma (accepted that the processes may separate prions but this could not be validated, therefore theoretical risk of vCJD remains)
13 May 98	DH Press Release (R0965-01) reporting CSM advice: UK fractionators to source plasma from outside UK
Apr 98	BPL begin quality audits of potential US plasma suppliers
May-Jun 98	UK fractionators shutdown manufacture from UK plasma; cleaning & decontamination of plant; submit PLVs for all products
17 Jul 98	DH Press Release 98/295 confirming acceptance of SEAC advice on leucodepletion
Jun-Aug 98	UK fractionators manufacture commissioning batches from US plasma collected pre-MCA audit of suppliers; MCA inspection of decontaminated UK facilities; US plasma suppliers satisfy MCA
27 Aug 98	DH Press Release (98/351) reporting the finding of vCJD prion protein in the appendix of a patient who went on to develop the disease

Aug 98 - Jan 99	UK fractionators manufacture fractionated plasma products from US plasma to create inventory
Dec 98 - Jan 99	UK fractionators release and issue fractionated plasma products from US plasma
Jan 99	World Federation of Hemophilia monograph "*Creutzfeldt-Jakob Disease and Haemophilia: Assessment of Risk*" – pragmatic review by Bruce Evatt, concludes "*... doctors and patients must weigh the unknown, but likely small, risk of CJD against the unavoidable, known, dangers of not receiving treatment. In most cases the answer is obvious.*"
Feb 99	Publication of the DNV Report "Assessment of the Risk of Exposure to vCJD Infectivity in Blood and Blood Products" (Final – Rev. 4)
Feb 99	"Recover and replace" activity to ensure UK plasma-derived product does not remain in indefinite use (not a formal recall)
May 99	Release and issue of anti-D immunoglobulin (IgG) derived from US plasma
Jul 99	Release and issue of HBs IgG and V-Z IgG from US plasma
Aug 99	Release and issue of tetanus IgG derived from US plasma
1 Nov 99	Only leucodepleted components manufactured by UK Transfusion Centres from this date
23 Nov 99	CBER "Guidance for Industry" on "*Revised Precautionary Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and New Variant Creutzfeldt-Jakob Disease (nvCJD) by Blood and Blood Products*" – provides the agency's current thinking; distinguishes between CJD (no recall of plasma products) and vCJD (recall); requires advice to consignees – recipient notification subject to clinical judgement
Dec 99	Release and issue of rabies IgG derived from US plasma
12 Jan 00	Letter DH to NBA (copied to territorial offices) confirming advice of PL(CO)(98)1 on recipient notification still effective but under active review
25 Jan 00	First meeting of the DH "Expert Group on the Management of CJD Incidents", under the chairmanship of Prof Don Jeffries
28 Apr 00	DH Press Release 2000/0250 reporting first (negative) findings from the survey of human tissues
17 Jul 00	DH Press Release following SEAC Meeting of 17 July 2000: with 76 "definite" and 7 "probable" cases of vCJD, the Committee concluded a significant rising trend (20%-30% p.a.)
8 Dec 00	BPL incident reference 11723/3: notification to consignees (UK and overseas) of plasma products affected by a definite vCJD donor
3 Jan 01	Monthly CJD statistics reflect 81 "definite" and 7 "probable" cases of vCJD

[i] *Lancet* 1997; 350:1704