UKHCDO

United Kingdom Haemophilia Centre Doctors' Organisation

7th September 2004

To UK Haemophilia Centre Doctors

Variant Creutzfeldt-Jakob Disease (vCJD) and Plasma Products

Dear Colleague,

We write to inform you that the Bio Products Laboratory (BPL) and Protein Fractionation Centre, Scotland (PFC) will shortly be releasing particular batch numbers for clotting factors (factor VIII and factor IX), antithrombin and other products manufactured using donations from individuals who subsequently developed vCJD.

These batches refer to plasma products, other than cryoprecipitate and fresh frozen plasma, sourced from UK donors until 1998, and include some batches that have been previously notified to consignees and some that have been traced subsequently. None of the implicated batches is within shelf life.

Previous notifications of UK donors who later developed vCJD, in 1997, 1999 and 2000, resulted in some recipients of implicated plasma products being traced but not put in an 'at-risk' group for vCJD. Following the announcement in December 2003 of a transfusion-associated case of vCJD, the situation regarding vCJD and plasma products has changed. Certain special precautions will need to be taken for some recipients of UK-sourced plasma products who may have been exposed to potential vCJD infectivity. This is in order to reduce any possible risk of onward transmission of vCJD.

Implicated batches

The basis for managing this notification is a detailed assessment of potential vCJD infectivity in implicated plasma products. This has been undertaken by the Health Protection Agency with the CJD Incidents Panel (CJDIP), an expert committee set up on behalf of the UK Chief Medical Officers to advise on the management of 'incidents' of potential transmission of CJD between patients. The Recommendations of the CJD Incidents Panel are enclosed.

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Nine UK plasma donors are now known to have developed vCJD. Collectively, they have made 23 plasma donations. The donated plasma has been used to manufacture factor VIII, factor IX, antithrombin, intravenous immunoglobulin G, albumin, intramuscular human normal immunoglobulin and anti-D.

Potential vCJD infectivity of plasma products

The potential risk of vCJD infection following treatment with any implicated plasma products, on top of the risk from dietary exposure to the bovine spongiform encephalopathy (BSE) agent, is very uncertain. However some patients treated with plasma products between 1980 and 2001 could pose a potential risk to others in defined circumstances.

The CJDIP advises that patients who are exposed to a 1% or greater potential additional risk of infection, should be considered 'at-risk' of vCJD for public health purposes (i.e. certain special precautions need to be taken to reduce any possible risk of onward transmission of vCJD).

Treatment with UK-sourced factor VIII (where the plasma concentrate used in the manufacturing process has been implicated), factor IX or antithrombin is highly likely to expose patients to this potential additional risk. This is because a single dose of these products, as used in clinical practice, is estimated to contain sufficient potential vCJD infectivity to cross the 1% threshold. Treatment with factor VIII where only the albumin excipient used in the manufacturing process, and not the plasma concentrate, has been implicated, is very unlikely to expose patients to a 1% or greater potential additional risk. This is because several thousand vials of the implicated product would be needed, and this is not likely to occur in clinical practice.

These calculations are based on very cautious assumptions, and take a precautionary approach in an area of much scientific uncertainty. Therefore the 1% threshold is a tool for limiting the possible risk of transmitting vCJD between patients and should **NOT** be seen as a way of estimating an individual patient's potential additional risk of developing vCJD.

It is likely that many patients with bleeding disorders1 will have been exposed to a potential additional risk of 1% or greater. It is also likely that further batches of UK-sourced plasma products will be implicated in the future as more cases of vCJD arise. For these reasons UK Haemophilia Doctors and patient representatives believe that **all patients with bleeding disorders[1] who have been treated with UK-sourced pooled factor concentrates or antithrombin[2] between 1980 and 2001[3] should be considered 'at-risk' of vCJD for public health purposes and special precautions taken.** The CJDIP and UK Health Departments have endorsed this approach.

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[1] defined here as congenital and acquired haemophilia (Haemophilia A and Haemophilia B), Von Willebrand Disease, other congenital bleeding disorders and congenital antithrombin III deficiency.

[2] ie. clotting factors and antithrombin made from pooled plasma. These include factor VIII, factor IX, factor VII, factor XI, factor XIII and prothrombin complex concentrates as well as antithrombin.

[3] The start date of 1980 is when BSE is thought to have entered the human food chain. The end date of 2001 is the last possible expiry date of any product manufactured by the UK fractionators that was sourced from UK donors until 1998.

Information for patients

All patients with bleeding disorders should be made aware of whether they have received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001.

All patients who have received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001 should:

a) Be informed that they are at a potential additional risk of vCJD because they may have been treated with plasma made from donations from individuals who have subsequently developed vCJD, or who will do so in the future.

b) Be given the opportunity to find out whether or not they received known implicated batches. This includes both batches that are highly likely to expose patients to a 1% or greater potential additional risk, as well as batches for which this likelihood is so low as to be considered negligible[4]. They should also be made aware that with future recognition of implicated batches, any assessment of their individual exposure might change. Whatever their choice, this information will not affect their management as the same special public health precautions will be taken for **ALL** patients who have received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001.

c) Be informed that they are considered 'at-risk' of vCJD for public health purposes, and that their 'at-risk' status will be recorded in their hospital medical records and primary care notes. The extent of exposure to implicated batches, and whether or not a patient has asked to know if they have received implicated batches, will also be recorded on a Patient vCJD Exposure Assessment Form (see below) to be placed in their hospital medical records. Patients who have **NOT** received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001 should also have this fact clearly recorded on this form.

d) Be informed that special precautions need to be taken to reduce the chance of any further spread of vCJD, and given the following advice:

   - They should not donate blood, organs or tissues (many patients who have received plasma products may already be excluded from donation because of their underlying condition)

   - They should inform any clinicians and other healthcare professionals with whom they have dealings of their 'at-risk' status, so that special infection control precautions can be taken before surgery and other invasive procedures should they require future medical care. Patients should also be advised to inform their families, in case the patient needs emergency surgery in the future (see Clinical Information document).

e) Be reassured that their clinical care should not be compromised in any way.

[4] Refer to vCJD Implicated Batch Numbers Tables 1 and 3, accompanying the 'Recommendations of the CJD Incidents Panel'.

Parallel arrangements are underway with clinicians caring for patients with other conditions (see Summary of patient notification exercise attached).

For patients treated with single unit blood components (red blood cells, platelets, cryoprecipitate or fresh frozen plasma) donated by people who subsequently developed vCJD these steps are already in place. Patients treated with vCJD implicated single unit blood components are identified by the UK national blood services and the National CJD Surveillance Unit, Edinburgh. Local health teams are then advised to contact these patients so they can take special public health precautions.

Batch details

Details of the batch numbers of **ALL** known plasma products manufactured using donations from people who subsequently developed vCJD, including batches previously notified, are listed in the Tables attached (see vCJD Implicated Batch Numbers Tables 1 to 3). These include details of all implicated batches of factor VIII, factor IX and antithrombin, as well as other products used to treat other clinical conditions, stratified according to potential 'risk'.

A list of the specific **subset** of implicated plasma products that are known to have been supplied to your centre will also be forwarded from the plasma product suppliers (BPL), via the manufacturers' consignees. PFC has notified its implicated factor VIII and factor IX batches to Haemophilia Centre Doctors previously, there are no new batches to notify at present and therefore PFC will not be forwarding further information at this time.

In some cases this information may not be available for a number of weeks or may be incomplete, because other distributors may be involved in the supply chain and need to hand search paper archives.

What we are asking you to do now

We are asking you to help implement the notification process described above. In order for the notification process to run as smoothly as possible, it is suggested that each haemophilia centre now takes the following actions:

1) Informing your staff

This information should be communicated to clinicians and other staff in your centre as appropriate. It is suggested each haemophilia centre identifies a lead clinician responsible for liaison and managing this incident locally, and a deputy in the event of absence of the lead.

2) Contacting all patients

A letter should now be prepared for **ALL** patients with bleeding disorders[1] who are or have been treated with pooled factor concentrates or antithrombin. We have enclosed a draft patient letter that we recommend be used for all patients, including those who may not be considered 'at-risk' for public health purposes, with an accompanying 'Information for Patients' sheet.

Please try to ensure that all patients are given this information and the opportunity to discuss this with you. You may wish to give patients the option to attend a clinic to discuss their potential exposure with adequate time and support to discuss these issues.

3) Timing

The UKHCDO together with the Health Protection Agency, Scottish Centre for Infection and Environmental Health, Department of Health (England), Welsh Assembly Government, Department of Health, Social Services and Public Safety (Northern Ireland) and Scottish Executive Health Department ask you to prepare to send out your letter to patients on **Monday 20th September** by first class post, so that patients will start receiving their letters on Tuesday 21st September. A national announcement from the Department of Health is planned for shortly after this date. The Haemophilia Society will have written to its members and made a vCJD factsheet available on its website by the end of this week.

Coordinating the communication exercise in this way will help to ensure that the different patient groups who need to be contacted receive their information as far as possible at the same time. Clinicians who choose to make different local arrangements for informing and contacting their patients need to be prepared to manage enquiries from them if they become aware of the information from other sources.

It is possible that some enquiries may arise from members of the public and patients in the period before those affected by the notification receive their letters. We enclose an 'Enquirer Handling Protocol' that aims to set out information and arrangements for handling such enquiries. We suggest the level of information contained in this document should be adequate to handle these enquiries until most affected patients have received their individual letters.

All media enquiries should be referred to the relevant Government Press Office (see Media Handling Protocol attached).

4) Identifying patients 'at-risk' of vCJD for public health purposes

Please identify which of your patients have received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001. These will constitute the group 'at-risk' of vCJD for public health purposes, for whom special precautions should be taken. Patients' 'at-risk' status should be recorded in their hospital and GP medical notes (see points 5 and 6 below).

If there is uncertainty about whether a patient has received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001 (eg due to incomplete records), then the patient should NOT be considered at risk of vCJD for public health purposes.

Patients who have died within the last year should also be assessed, and if identified as 'at risk', have their clinical history reviewed in order to identify and manage any recent surgical incident that may pose an infection control risk. Should centres identify 'at-risk' patients who are currently treated elsewhere, the centre doctor

should contact the clinician currently responsible for the patient's care, so they may manage the patient appropriately.

5) Patient vCJD Exposure Assessment

A Patient vCJD Exposure Assessment Form is attached to record the extent of exposure of individual patients to implicated products. You will need to identify which of your patients has received the implicated batches. Once completed, this form should be retained in the patient's hospital notes.

Population information on the extent of exposure of individual haemophilia patients is vital for public health monitoring and to inform public health precautions and future policy for this patient group. For this reason, a photocopy of each form should be forwarded as soon as possible after completion, in confidence to the UKHCDO National Haemophilia Database Co-ordinator in Manchester (address on form). This information is recorded anonymously, using only the patient's UKHCDO National Registration Number and date of birth. Therefore the patient's name should not be provided on the copy of the form that is forwarded.

6) Contacting GPs

The clinician responsible for a patient who is 'at-risk' of vCJD for public health purposes should contact that patient's general practitioner so they may:

- know that their patient is being informed about their 'at-risk' status,
- record the patient's 'at-risk' status and the special precautions required in their primary care records,
- include this information in any referral letters should the patient require surgery or other invasive medical procedures (see point 7.below)
- check information on the patient's recent surgical history at other hospitals and, if they have, liaise with their local Health Protection Team in order to ascertain whether any further action needs to be taken (see point 7.below)

We enclose a draft GP letter that we recommend be used for this purpose.

7) Infection Control

Please inform your Director of Infection Control (England) or Senior Infection Control Manager (HDL(2001)10) (Scotland) about any patients who are 'at-risk' of vCJD for public health purposes so that the appropriate special precautions may be taken. Guidance on infection control for any patient who is considered 'at-risk' of vCJD was published by the ACDP TSE Working Group in 2003: http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/Index.htm.

As well as ensuring that infection control procedures are in place for any 'at-risk' patients who require surgery, the Director of Infection Control (England) or Senior Infection Control Manager (HDL(2001)10) (Scotland) should report relevant past surgical incidents to the CJDIP. If your patient has undergone surgery within the past 12 months please liaise with the local Infection Control Team in order to ascertain whether any further action needs to be taken.

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VCJD IMPLICATED BATCH NUMBERS

Table 1: Products where the likelihood of a recipient surpassing the threshold dose for public health purposes is HIGH[1,2].
THESE BATCHES SHOULD BE TRACED, THE INDIVIDUAL RECIPIENTS CONSIDERED 'AT-RISK' OF VCJD FOR PUBLIC HEALTH PURPOSES, AND SPECIAL PUBLIC HEALTH PRECAUTIONS TAKEN

Factor VIII				Factor IX				Antithrombin			
Brand name	Vial Size (iu)	Batch Number	Release date	Brand name	Vial Size [iu]	Batch Number	Release date	Brand name	Vial Size [iu]	Batch Number	Release Date
8Y	500	FHB4116	26.06.92	9A	600	FJA0092	24.05.90	Antithrombin*	500	ATA4535*	20.12.96
8Y	500	FHB4189	14.04.93	9A	600	FJA4239B	09.07.93				
8Y*	500	FHB4419*	31.07.95	9A	600	FJA4308	18.06.94				
8Y*	500	FHB4547*	01.11.96								
8Y*	500	FHB4596*	06.05.97	Replenine	500	FJM4327	10.10.94				
				Replenine	500	FJM4437	27.11.95				
8Y	250	FHC0289	23.05.90	Replenine*	500	FJM4596*	23.04.97				
8Y	250	FHC0369	18.12.90	Replenine	500	FJM4625	07.07.97				
8Y	250	FHC4237	09.03.94								
				HT DEFIX (PFC)	276	3502-70210	14.09.87				
Replenate	500	FHE4437	21.09.95								
Replenate*	500	FHE4536*	04.09.96								
Replenate*	500	FHE4548*	17.10.96								
Replenate	1000	FHF4625	29.07.97								
High purity F8	500	FHM3990	17.11.91								
High purity F8	500	FHM4054	06.05.92								
Z8 (PFC)	160	0301-70320	02.08.87								
Z8 (PFC)	190	0304-70510	14.07.87								
Total		16		Total		8		Total		1	

[1] All products implicated to date: including batches previously notified to consignees(*)
[2] All products manufactured in UK: products manufactured by the Protein Fractionation Centre, Scotland are designated 'PFC'. All other products manufactured by Bio Products Laboratory.

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VCJD IMPLICATED BATCH NUMBERS

Table 2: Products where the likelihood of a recipient surpassing the threshold dose for public health purposes is MEDIUM [1,2].
EFFORTS SHOULD BE MADE TO TRACE THESE BATCHES AND TO ASSESS THE POTENTIAL ADDITIONAL RISK TO INDIVIDUAL RECIPIENTS OF vCJD INFECTION TO DETERMINE IF SPECIAL PUBLIC HEALTH PRECAUTIONS SHOULD BE TAKEN.

Intravenous Immunoglobulin				Albumin 4.5%			
Brand name	Vial Size (g)	Batch Number	Date of release	Brand name	Vial Size (ml)	Batch Number	Date of release
Vigam S	5	VGC018	20.04.94	Albumin 4.5%	500	ADA0232	27/06/1991
Vigam S	5	VGC018A	12.05.95	Albumin 4.5%	500	ADA0233	28/06/1991
Vigam S*	5	VGC047*	19.12.96	Albumin 4.5%	500	ADA0234	28/06/1991
Vigam S*	5	VGC048*	20.01.97	Albumin 4.5%	500	ADA0387	11/08/1993
Vigam S*	5	VGC049*	30.01.97	Albumin 4.5%	500	ADA 390	15/09/1993
Vigam S	5	VGC085	14.11.97	Albumin 4.5%*	500	ADA0529*	11/07/1995
Vigam S	5	VGC087	21.11.97	Albumin 4.5%	500	ADA0629	14/08/1996
Vigam S	5	VGC110	09.04.98	Albumin 4.5%	500	ADA0631	14/08/1996
Vigam S	5	VGC11:	14.05.98	Albumin 4.5%*	500	ADA0680*	08/05/1997
				Albumin 4.5%	500	ADA0763	14/09/1998
Vigam S*	2.5	VGD050*	14.03.97				
				Albumin 4.5%	250	ADB0163	22/08/1990
Vigam L	5	VLC088	05.01.98	Albumin 4.5%	250	ADB0441	12/05/1994
				Albumin 4.5%*	250	ADB0681*	02/05/1997
				Albumin 4.5%	250	ADB0751	08/04/1998
				Albumin 4.5%	100	ADC0443	18/05/1994
				Albumin 4.5%	50	ADD0632	14/10/1996
				SPPS (PFC)	400	3301-81930	22/03/1988
				SPPS (PFC)	400	3301-81940	11/03/1988
				SPPS (PFC)	400	3301-81990	31/10/1988
				SPPS (PFC)	400	3302-71150	30/04/1987
				SPPS (PFC)	400	3302-71160	08/05/1987
				SPPS (PFC)	400	3302-71170	08/05/1987
				SPPS (PFC)	400	3302-71190	08/05/1987
				SPPS (PFC)	400	3305-71400	19/08/1987
				SPPS (PFC)	400	3305-71410	30/07/1987
				SPPS (PFC)	400	3305-71420	19/08/1987
				SPPS (PFC)	400	3305-71435	21/08/1987
				SPPS (PFC)	400	3312-71920	11/03/1988
Total		11		Total		28	

[1] All products implicated to date: including batches previously notified to consignees(*)
[2] All products manufactured in UK: products manufactured by the Protein Fractionation Centre, Scotland are designated 'PFC'. All other products manufactured by Bio Products Laboratory.

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VCJD IMPLICATED BATCH NUMBERS

Table 3: Products where the likelihood of a recipient surpassing the threshold dose for public health purposes is LOW[1,2], THESE BATCHES DO NOT NEED TO BE TRACED AND THE INDIVIDUAL RECIPIENTS DO NOT NEED TO BE INFORMED.

Albumin 20%			Factor VIII (excipient implicated)			Factor VIII (excipient implicated)			Intramuscular Immunoglobulins		
Brand name	Vial Size (ml)	Batch Number	Brand name	Vial Size (iu)	Batch Number	Brand name	Vial Size (iu)	Batch Number	Brand name	Vial Size (mg)	Batch Number
Albumin 20%	100	ABC0065	Replenate	250	FHD4235	High purity Factor 8	500	FHM4200	Normal	750	GGB064
Albumin 20%	100	ABC0111	Replenate	250	FHD4247B	High purity Factor 8	500	FHM4202			
Albumin 20%	100	ABC0157	Replenate	250	FHD4267B	High purity Factor 8	500	FHM4206	Normal	250	GGD077
Albumin 20%	100	ABC0219	Replenate	250	FHD4267C	High purity Factor 8	500	FHM4209	Normal	250	GGD084F
Albumin 20%	100	ABC0229	Replenate*	250	FHD4579*	High purity Factor 8	500	FHM4210	Normal	250	GGD084G
Albumin 20%	100	ABC0233				High purity Factor 8	500	FHM4211	Normal	250	GGD084H
Albumin 20%	100	ABC0237	Replenate	500	FHE4218	High purity Factor 8	500	FHM4212	Normal	250	GGD085
Albumin 20%	100	ABC0246	Replenate	500	FHE4244B	High purity Factor 8	500	FHM4214	Normal	250	GGD086
Albumin 20%*	100	ABC0360*	Replenate	500	FHE4247A	High purity Factor 8	500	FHM4216	Normal	250	GGD130
Albumin 20%	100	ABC0399	Replenate	500	FHE4250	High purity Factor 8	500	FHM4217	Normal	250	GGD131
			Replenate	500	FHE4267A	High purity Factor 8	500	FHM4219			
Albumin 20%	50	ABD0290	Replenate	500	FHE4277A	High purity Factor 8	500	FHM4220	IMIgG (PFC)	745	0709-70190
Albumin 20%	50	ABD0291	Replenate	500	FHE4277B	High purity Factor 8	500	FHM4221			
Albumin 20%	50	ABD0295	Replenate	500	FHE4286	High purity Factor 8	500	FHM4223	Anti-D	500	GDC071
Albumin 20%*	50	ABD0311*	Replenate*	500	FHE4579*	High purity Factor 8	500	FHM4227	Anti-D	250	GDD072
Albumin 20%*	50	ABD0319*	Replenate	500	FHE4653	High purity Factor 8	500	FHM4229			
Albumin 20%*	50	ABD0324*	Replenate	500	FHE4658	High purity Factor 8	500	FHM4246			
Albumin 20%*	50	ABD0325*				High purity Factor 8	500	FHM4249			
Albumin 20%*	50	ABD0332A*	Replenate	1000	FHE4244C	High purity Factor 8	500	FHM4257			
Albumin 20%	50	ABD 389	Replenate	1000	FHF4244C	High purity Factor 8	**500**	**FHM4259**			
Albumin 20%	50	ABD0445	Replenate	1000	FHF4252	High purity Factor 8	500	FHM4261			
Albumin 20%	50	ABD0458	Replenate*	1000	FHF4577*	High purity Factor 8	500	FHM4262			
						High purity Factor 8	500	FHM4263			
			High purity Factor 8	500	FHM4127	High purity Factor 8	500	FHM4268			
			High purity Factor 8	500	FHM4136	High purity Factor 8	500	FHM4272			
			High purity Factor 8	500	FHM4136A	High purity Factor 8	500	FHM4275			
			High purity Factor 8	500	FHM4138	High purity Factor 8	500	FHM4278			
			High purity Factor 8	500	FHM4140	High purity Factor 8	500	FHM4281			
			High purity factor 8	500	FHM4142	High purity Factor 8	500	FHM4290			
			High purity Factor 8	500	FHM4144	High purity Factor 8	500	FHM4297			
			High purity Factor 8	500	FHM4148						
			High purity Factor 8	500	FHM4160	High purity Factor 8	1000	FHP4161			
			High purity Factor 8	500	FHM4163	High purity Factor 8	1000	FHP4197			
			High purity Factor 8	500	FHM4164	High purity Factor 8	1000	FHP4213			
			High purity Factor 8	500	FHM4173	High purity Factor 8	1000	FHP4245			
			High purity Factor 8	500	FHM4182	High purity Factor 8	1000	FHP4255			
			High purity Factor 8	500	FHM4183	High purity Factor 8	1000	FHP4265			
			High purity Factor 8	500	FHM4184	High purity Factor 8	1000	FHP4279			
			High purity Factor 8	500	FHM4185	High purity Factor 8	1000	FHP4296			
			High purity Factor 8	500	FHM4186						
			High purity Factor 8	500	FHM4190	High purity Factor 8	250	FHR4175			
Total		21	Total		38	Total		39	Total		12

[1] All products implicated to date: including batches previously notified to consignees(*)
[2] All products manufactured in UK: products manufactured by the Protein Fractionation Centre, Scotland are designated 'PFC'. All other products manufactured by Bio Products Laboratory.