BPL

BPL CJD recalls documentation of involved products

Bio Products Laboratory

Memorandum

To: Pat Hewitt

In confidence

cc: Angela Robinson ✓

From: Terry Snape

Date: 05/01/00

Subject: vCJD - product batches affected

Our ref: VCJD-RPDI

Ext. No.: 2436

RECEIVED
- 6 JAN 2000

Pat:

Grovelling apologies for taking so long to respond to your request for information for Bob Will – no real excuse I'm afraid, the reports were precompiled, your e-mail just got pushed out of sight by things that had to be done yesterday.

I have attached two copies of a set of three summary reports. By all means forward one set direct to Bob Will.

The significant detail is all in the first report (covering notifications up to 31 December 1997) – no subsequent reports have led to implicated batches. The list of affected batches is a long one, primarily because one of the batches of albumin (ABC0065) was used as excipient in the manufacture of factor VIII over an 18 month period. ***Replenate***™ is monoclonal antibody purified factor VIII made on site at Elstree; 8SM was the same product manufactured for BPL under contract by Kabi Pharmacia. There were good reasons why it made sense to assign a single batch of albumin for this purpose; the practice was discontinued in the light of these findings.

There are several facets to these circumstances affecting factor VIII. The albumin excipient constitutes most of the protein in the factor VIII concentrate; on the other hand albumin is probably the lowest risk product in any calculation of risk; the dose volume – and therefore the albumin dose – is very small; severely affected haemophiliacs receive regular treatment throughout their lives. These facts, and others, were incorporated into the DNV risk assessment report.

All three reports were copied to DoH, MCA and NBA/NBS, as well as necessary circulation at BPL; otherwise, the policy of not advising recipients of affected products was followed. I'm not sure how Bob plans to use the information but it would be important that BPL had early notification of any intention to disseminate/publish the information more widely. He should contact me in this regard.

Best regards,

GRO-C

Terry Snape,
Technical Director (BPL).

BPL

Report on C-JD Post Donation Notifications

Notifications up to 30 June 1998

Confidential Report

Report generated by:

GRO-C

S.J. Jenkins
Quality Assurance Manager

Copies supplied in confidence to:

BPL	Executive members
DOH	Dr. J Metters
	Dr. M. McGovern
MCA	Dr. F. Rotblat
	Mr. N Goulding
	Dr M. Kavanagh
NBS	Dr. P. Flanagan
NBA	Dr. A. Robinson

BPL Quality Control
DATE 7 - AUG 1998
ACTION
FILING

Introduction

This report summarises notifications. received by BPL in the last quarter, of plasma donations subsequently implicated due to information relating to an episode or risk of C-JD. Previous notifications are detailed in reports numbered CJDREP12 and CJDRP981. Classical / familial C-JD implicated donations are traced only for donations received after September 1991(a convenient cut-off date since the implementation of HCV-Ab screening at that time ensures that no products from earlier donations will still be in use).

New Variant C-JD Notifications

There have been no further notifications of donations implicated by nvC-JD.

Classical / Familial C-JD Notifications

Between the end of March and June there were no more notifications. There has been one recent notification from Brentwood of over 200 donations which fall into the risk categories for C-JD. Further information is being sought and will be detailed in the next quarter's report.

GRO-C

S.J. Jenkins
Quality Assurance Manager
30 July 1998

BPL

Report on C-JD Post Donation Notifications

Notifications up to 31March 1998

Confidential Report

Report generated by:

GRO-C

S.J. Jenkins
Quality Assurance Manager

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	Dr. M. McGovern
MCA	Dr. F. Rotblat
	Mr. N Goulding
	Dr M. Kavanagh
NBS	Dr. P. Flanagan
NBA	Dr. A. Robinson

Introduction

This report summarises notifications to BPL in the last quarter of plasma donations subsequently implicated due to information relating to an episode or risk of C-JD. Previous notifications are detailed in report number CJDREP98 dated 6/1/98. Classical / familial C-JD implicated donations have been traced only for donations received after September 1991(a convenient cut-off date since the implementation of HCV-Ab screening at that time ensures that no products from earlier donations will still be in use).

New Variant C-JD Notifications

There have been no further notifications of donations implicated by nvC-JD.

BPL was made aware that there was one donor with suspected nvC-JD but this was later confirmed not to be C-JD.

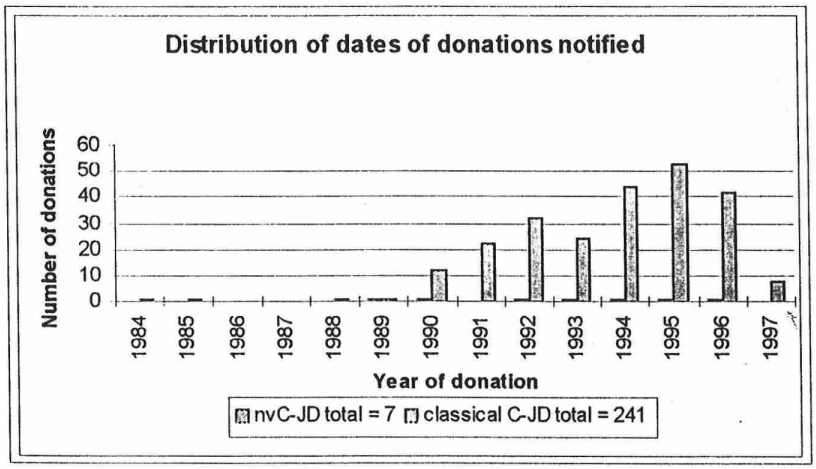
Dr. Snape has also reported to the MCA a case where a patient who has been confirmed as having nvC-JD was thought by the family to be a donor. No evidence has been found that this person has ever donated blood or plasma to the service after extensive searches by the NBS.

Classical / Familial C-JD Notifications

Up to the end of March 1998 BPL had received notifications of a further 124 donations implicated due to risk of C-JD. The donations received after September 1991 are being traced to plasma pools, most are complete, some traces have yet to be completed on donations most recently notified. No further action will be taken once the traces are complete.

One donor had been treated by growth hormone therapy, two donors (7 donations) had received corneal grafts.

No notifications have categorically stated that the donor subsequently developed classical C-JD.



S.J. Jenkins
Quality Assurance Manager
9 April 1998

BPL

Report on C-JD Post Donation Notifications

Notifications up to 31 December 1997

Confidential Report

Report generated by:

GRO-C

S.J. Jenkins
Quality Assurance Manager

Copies supplied in confidence to:

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DOH	Dr. J Metters
	Dr. M. McGovern
MCA	Dr. F. Rotblat
	Mr. N Goulding
NBS	Dr. P. Flanagan
NBA	Dr. A. Robinson

Introduction

This report summarises notifications to BPL of delivered plasma donations subsequently implicated due to information relating to an episode or risk of C-JD. The report is divided into 2 sections, reports and trace results on nvCJD, numbers of donations implicated by familial / classical C-JD affected donors. The total number of donations notified to BPL is reported for each section, in the case of classical / familial C-JD the traces have only been undertaken for donations received after September 1991(a convenient cut-off date since the implementation of HCV-Ab screening at that time ensures that no products from earlier donations will still be in use).

New Variant C-JD Notifications

Up to the end of December 1997 BPL has been notified of 7 donations obtained from 3 donors who subsequently developed nvC-JD. One of these was donated in January 1990; insufficient information is available to trace the plasma start pool.

The following products were manufactured from the 6 other start pools, or incorporated implicated albumin as an excipient, and released for sale or for clinical trial use.

Table 1. Batches produced from nvC-JD implicated pools

Dose/ strength	Batch number	Expiry date	Number released	Dose/ strength	Batch number	Expiry date	Number released
Human Albumin Solution, Zenalb 20%							
100ml	ABC0065	1/4/95	2971	50ml	ABD0295	11/9/97	8805
100ml	ABC0111	5/1/95	4314	50ml	ABD0319[1]	6/8/98	9043
100ml	ABC0219	18/11/96	4220	50ml	ABD0324[1]	4/9/98	9203
100ml	ABC0229	7/12/96	4269	50ml	ABD0325[1]	5/9/98	8654
50ml	ABD0290	13/8/97	8625	50ml	ABD0332A[1]	5/8/98	8174
50ml	ABD0291	14/8/97	8837				
Human Albumin Solution, Zenalb 4.5%							
500ml	ADA0387	30/6/96	4022	500ml	ADA0529[1]	14/11/97	3826
500ml	ADA0390	26/7/96	3323	250ml	ADB0163	30/5/93	3167
Human Normal Immunoglobulin, intramuscular							
750mg	GGB064	19/11/93	4229	250mg	GGD085	9/12/94	17205
250mg	GGD077	14/1/95	19106	250mg	GGD086	18/12/94	16585
250mg	GGD084F	9/11/94	5421	250mg	GGD130	21/5/96	18323
250mg	GGD084G	9/11/94	17903	250mg	GGD131	18/6/96	19252
250mg	GGD084H	9/11/94	5000				
Human Anti-D Immunoglobulin, intramuscular							
500iu	GDC071	2/11/96	19685	500iu	GDC072	26/1/97	8931
Factor VIII, Type 8Y							
500iu	FHB4116	9/4/95	1476	250iu	FHC0289	1/3/93	2481
500iu	FHB4419[1]	6/6/98	1988	250iu	FHC4237	4/10/96	4982
500iu	FHB4547[1]	19/9/97	1789				

Table 1 continued

Dose/ strength	Batch number	Expiry date	Number released	Dose/ strength	Batch number	Expiry date	Number released
Factor VIII. Replenate							
250iu	FHD4235[2]	24/8/96	3363	500iu	FHE4267A [2]	30/8/96	1060
250iu	FHD4247B[2]	5/9/96	3445	500iu	FHE4277A [2]	14/12/95	2202
250iu	FHD4267B[2]	1/3/96	2380	500iu	FHE4277B [2]	21/12/95	1309
250iu	FHD4267C[2]	25/4/96	1491	500iu	FHE4286 [2]	16/12/95	4041
500iu	FHE4218	17/6/94	1634	500iu	FHE4548[1]	2/9/98	3321
500iu	FHE4244B[2]	4/10/94	1106	1000iu	FHF4244C [2]	4/10/94	608
500iu	FHE4247A[2]	18/8/96	1829	1000iu	FHF4252 [2]	5/9/96	1684
500iu	FHE4250[2]	5/9/96	3173				
Factor VIII. 8SM [2]							
250iu	FHR4175	16/11/95	3360	500iu	FHM4217	17/5/96	1623
500iu	FHM4127	4/6/95	1698	500iu	FHM4219	22/6/96	1637
500iu	FHM4136	8/6/95	2112	500iu	FHM4220	28/6/96	3035
500iu	FHM4136A	11/6/95	1603	500iu	FHM4221	5/7/96	2966
500iu	FHM4138	17/8/95	1601	500iu	FHM4223	30/6/96	1412
500iu	FHM4140	20/8/95	1865	500iu	FHM4227	9/9/96	1626
500iu	FHM4142	21/9/95	1844	500iu	FHM4229	16/8/96	1695
500iu	FHM4144	24/9/95	1930	500iu	FHM4246	28/9/96	1428
500iu	FHM4148	14/9/95	1751	500iu	FHM4249	3/10/96	1400
500iu	FHM4160	28/9/95	1989	500iu	FHM4257	21/10/96	1347
500iu	FHM4163	21/10/95	1750	500iu	FHM4259	24/10/96	1568
500iu	FHM4164	26/10/95	2003	500iu	FHM4261	26/10/96	1461
500iu	FHM4173	21/11/95	1776	500iu	FHM4262	2/11/96	1454
500iu	FHM4182	7/2/96	2109	500iu	FHM4263	16/11/96	1386
500iu	FHM4183	7/12/95	1946	500iu	FHM4268	14/11/96	1395
500iu	FHM4184	31/12/95	1687	500iu	FHM4272	5/12/96	2909
500iu	FHM4185	1/2/96	2039	500iu	FHM4275	16/12/96	1400
500iu	FHM4186	4/2/96	1970	500iu	FHM4278	20/1/97	1579
500iu	FHM4190	31/12/95	1681	500iu	FHM4281	3/2/97	1582
500iu	FHM4200	31/12/95	1771	500iu	FHM4290	13/2/97	681
500iu	FHM4202	31/12/95	1799	500iu	FHM4297	24/2/97	5692
500iu	FHM4206	31/12/95	1666	1000iu	FHP4161	29/10/95	879
500iu	FHM4209	31/12/95	2030	1000iu	FHP4197	11/3/96	931
500iu	FHM4210	31/12/95	1604	1000iu	FHP4213	6/5/96	862
500iu	FHM4211	31/12/95	1743	1000iu	FHP4245	14/9/96	697
500iu	FHM4212	4/5/96	1777	1000iu	FHP4255	31/10/96	687
500iu	FHM4214	31/12/95	1672	1000iu	FHP4265	2/12/96	689
500iu	FHM4216	9/9/96	1637	1000iu	FHP4279	1/2/97	791
				1000iu	FHP4296	15/2/97	1158
Factor IX. Type 9A							
600iu	FJA0092	16/4/91	798	600iu	FJA4239B	12/7/96	473

(1) = product recalled. (2) = ABC0065 used as excipient. Total units released = 388,109.

Table 2
Exported material from batches detailed in table 1

PRODUCT CODE	BATCH NUMBER	EXPIRY DATE	CUSTOMER	QTY	COUNTRY	DATE SUPPLIED
HNIG 250mg	GGD131	18/6/96	SOS BOSNIA	4000[1]	BOSNIA	14/3/96
Anti-D 500iu	GDC071	2/11/96	SEIF PHARMA	3040	EGYPT	3/10/95
						19/10/95
HAS 20% 50ml	ABD0324	4/9/98	SEIF PHARMA	5998	EGYPT	30/10/96 21/2/97
HAS 20% 50ml	ABD0325	5/9/98	SEIF PHARMA	144	EGYPT	21/2/96
HAS 20% 50ml	ABD0290	13/8/97	SEIF PHARMA	8625	EGYPT	30/5/96 27/9/96
HAS 20% 100ml	ABC0065	1/4/95	KABI	700[2]	SWEDEN	29/3/93
HAS 20% 50ml	ABD0291	14/8/97	MEIZLER	8817	BRAZIL	5/6/96 30/7/96
HAS 20% 50ml	ABD0295	11/9/97	MEIZLER	7802	BRAZIL	4/7/96 2/10/96 4/7/96
HAS 20% 50ml	ABD0319	6/8/98	MEIZLER	9005	BRAZIL	25/10/96
HAS 20% 50ml	ABD0324	4/9/98	MEIZLER	3205	BRAZIL	25/11/96
HAS 20% 50ml	ABD0325	5/9/98	MEIZLER	8510	BRAZIL	25/11/96 6/12/96 10/12/96
HAS 20% 50ml	ABD0332A	5/8/98	MEIZLER	3205	BRAZIL	25/11/96
HAS 20% 50ml	ABD0295	11/9/97	INCHCAPE	1000	SINGAPORE	10/7/96
HAS 20% 50ml	ABD0295	11/9/97	MUSCAT PHARMA	3[3]	OMAN	11/7/96
HAS 20% 100ml	ABC0111	5/1/95	PHARMA GLOBUS	3334	TURKEY	24/8/93 9/11/93 19/4/94 17/5/94 2/8/94 24/8/94 31/8/94 5/10/94

Recalls of extant material were undertaken as precautionary measures, and following discussions with the MCA and DOH.

Fraction 4 paste is a by-product of the albumin process. Some of the paste manufactured from the same plasma pools as the batches above has been sold. It is understood that the purchaser recovers albumin for clinical use from the paste. BPL has notified the purchaser about the two most recent implicated plasma pools, where it was considered possible that there may have been extant final products.

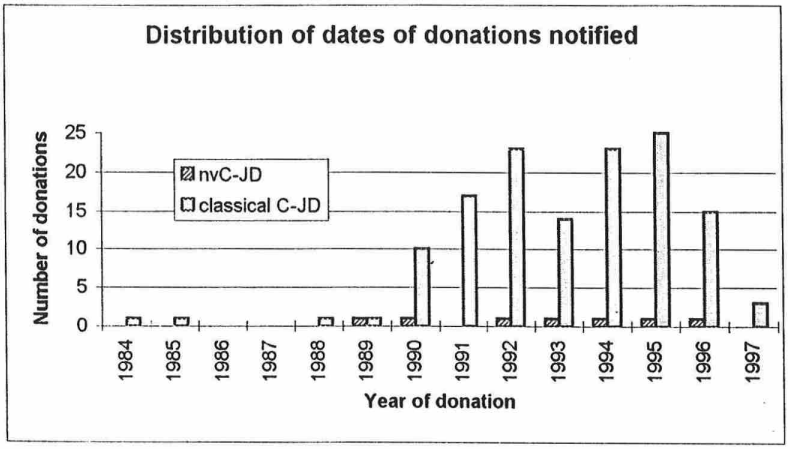
BPL can not provide definitive information on the use of albumin as excipients by other manufacturers as albumin is distributed through the normal pharmaceutical wholesale dealers as well as directly to customers. However it is known that ABD0332A was supplied to Nycomed Amersham, who used it as an excipient and also to Celltech, a biotechnology organisation.

Classical C-JD Notifications

Up to the end of December 1997 BPL had received notifications of 117 donations implicated due to risk of C-JD. Included in these are donations where a relative had developed nvC-JD. The donations received after September 1991 are being traced to plasma pools, most are complete, some traces have yet to be completed on donations most recently notified. No further action will be taken once the traces are complete.

One notification related to a donor who had received a scleral graft from an organ donor later found to have developed classical C-JD.

No notifications have categorically stated that the donor subsequently developed classical C-JD.



Comments

The number of final product containers implicated by the 6 nvC-JD related donations traced is greater than 388,000, of which 123,024 were human normal immunoglobulin vials.

All of the Factor VIII type 8SM batches and most of the Replenate batches were implicated due to incorporation of one implicated batch of Zenalb 20%, ABC0065. The practice of reserving a batch of albumin for excipient use has been stopped. Excipient use of any batch of albumin is limited to three batches of another product thus preventing such a multiplication of implicated batches. However it is not known whether the resultant patient risk, if any, is increased or decreased. The risk will be partly dependent on whether or not of diluting the albumin in the formulated batch reduces concentration of any infective agent to below an infective dose.

It is notable that there have been no notifications which have specifically stated that donors have subsequently developed classical C-JD. The mechanism and requirement for the donation Centres to report such incidents to BPL is in place. Therefore one has to conclude that either there have been no such cases or that the Centres have not been notified of them.

Progress of the two recalls, references P97/205 and P97/208, is detailed in separate reports. In summary it is clear that most of the product had already been used, a small number of vials of batches ABD0332A, FHE4548, and FHB4547 have been returned to BPL. Samples of all product batches are retained, BPL will keep samples of C-JD implicated batches indefinitely.

S.J. Jenkins
Quality Assurance Manager