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V10.3 (23/07/04)

vCJD AND IMPLICATED PLASMA PRODUCTS NOTIFICATION ROAD MAP

Contents

1. Background

In 1997, 1999 and 2000 the national blood services were advised of donors who later developed vCJD. The implicated products that had been manufactured from plasma donated by these donors were identified and consignees were notified according to guidance at the time. These earlier notifications did not involve placing patients in an "at risk" group for vCJD. However some recipients were traced and informed by their clinician.

The situation has changed. Regarding plasma products, the CJD Incidents Panel currently advises that certain public health 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. These new recommendations were not available at the time of previous notifications. In December 2003 the first possible transfusion-associated case of vCJD was announced, increasing concern regarding the potential vCJD infectivity of blood products.

To date, nine UK plasma donors are now known to have developed vCJD. 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.

2. Summary table of implicated batches (based on information supplied to 21.07.04)

(Likelihood of surpassing threshold) Product	Total batches*	BPL	PFC
(High)			
Factor VIII (intermediate)	16 (5)	14	2
Factor IX	8 (1)	7	1
Anti-thrombin	1 (1)	1	0
(Medium)			
Intravenous immunoglobulin	11 (4)	11	0
Albumin 4.5%	28 (3)	16	12
(Low)			
Albumin 20%	21 (6)	21	0
Intramuscular human normal immunoglobulin	10	9	1
Anti-D	2	2	0
Factor VIII (excipient)	77 (3)	77	0
Total implicated product batches	**174 (23)**		
(Intermediate)			
Fraction IV	12(5)	12	0
Fraction V	1	1	0
Cryoprecipitate	1	1	0

* parentheses indicate batches previously notified by BPL

3. Recommendations of the CJD Incidents Panel

July 2004

To Whom It May Concern:

Assessment of exposure to particular batches of variant Creutzfeldt-Jakob disease (vCJD) implicated plasma products

Recommendations of the CJD Incidents Panel

This letter sets out the recommendations of the CJD Incidents Panel (CJDIP)[1] for the tracing and assessment of patients exposed to plasma products manufactured in the UK using donations from individuals who subsequently developed vCJD.

The recommendations are based on a blood and blood products CJD Risk Assessment carried out by Det Norske Veritas Consulting [http://www.dnv.com/consulting/news_consulting/RiskofInfectionfromvariantCJDinBlood.asp] and accepted by the Spongiform Encephalopathy Advisory Committee (SEAC), the Committee on the Microbological Safety of Blood and Tissue, and by the Committee on Safety of Medicines. Batch specific manufacturing data from the fractionators concerned has been used with the Risk Assessment to estimate the potential vCJD infectivity in each batch of implicated product. For each of the major assumptions underlying the Risk Assessment, the most precautionary option was chosen.

The CJDIP has defined an "at-risk" threshold for public health purposes as the possibility of being exposed to a 1% or greater potential risk of infection, on top of the general risk to the UK population that is thought to have resulted from dietary exposure to the BSE agent. On this basis, three levels of likelihood of surpassing the threshold have been categorised as follows:

- **High:** the amount of vCJD potential infectivity is high enough for the threshold to be surpassed following the administration of a very small dose (e.g. one treatment with factor VIII, factor IX or antithrombin where one vial used has been implicated).

- **Medium:** the amount of potential vCJD infectivity is not low enough to be ignored but substantial quantities of the material in question would need to be administered before the threshold is surpassed (e.g. several infusions of implicated intravenous immunoglobulin, or large doses of implicated albumin 4.5%).

- **Low:** the amount of potential vCJD infectivity is so low that the likelihood of surpassing the threshold can realistically be ignored (e.g. implicated albumin 20%, factor VIII products using implicated albumin as an excipient, implicated intramuscular human normal immunoglobulin used for example for travel prophylaxis against hepatitis A, implicated anti-D.)

The threshold is a guide for implementing public health precautions to limit any possible human-to-human transmission of vCJD.

The uncertainties underlying the assessment of "risk" are great, and several precautionary assumptions are involved. Therefore, the "at-risk" threshold for public health purposes is not a precise guide for advising individuals about their potential additional risk of developing vCJD.

All batches of plasma products implicated to date have now been reviewed. This includes batches that were the subject of previous notifications. All the implicated products have passed their expiry date.

The CJDIP recommends the following action in relation to each implicated batch of plasma product, according to the likelihood that recipients will have surpassed the "at-risk" threshold for public health purposes:

High: These batches should be traced, the individual recipients considered at potential additional risk of vCJD infection, and "at-risk" for public health purposes. The extent of individual exposure to these batches should be documented.

Medium: Efforts should be made to trace these batches and to assess the potential additional risk to individual recipients to determine if precautions should be taken for public health purposes. The extent of individual exposure to these batches should be documented.

Low: These batches do **NOT** need to be traced and the individual recipients do not need to be informed. **The potential additional risk to recipients from particular implicated batches of albumin 20%, intramuscular human normal immunoglobulin, anti-D, and from factor VIII products manufactured using albumin that has been implicated as an excipient, is considered negligible.**

Help and information are supplied in additional documentation accompanying this recommendation. For each of these categories, the attached Annex to these Panel Recommendations provides a list of implicated batches of plasma products. This includes all plasma products implicated to date.

Professor Don Jeffries
Acting Chair
CJD Incidents Panel

Dr Nicky Connor
Medical Secretary
CJD Incidents Panel

1 The CJD Incidents Panel [http://www.hpa.org.uk/infections/topics_az/cjd/incidents_panel.htm.] is an expert committee established by the Chief Medical Officer in 2000. Its terms of reference include:

'To assist all those bodies responsible for the provision and delivery of healthcare to decide on the most appropriate action to take to handle incidents involving potential transmission of Creutzfeldt-Jakob Disease (CJD) and variant CJD (vCJD) between patients through clinical interventions, including via surgical instruments, tissues, organs and blood and to keep the relevant devolved administrations informed.

To consider what information should be collected on patients who may have been exposed; advise on what studies or follow-up may be needed; advise Directors of Public Health on patient tracing and notification exercises where these are indicated; and advise on whether any other measures are needed to protect the wider public health.'

4. Project Plan

4.1 Patients with bleeding disorders

"At-risk": All patients who have been treated with UK sourced factor VIII, factor IX or anti-thrombin beginning1980 to end 2001.

Information provided to Haemophilia Centre Director	Action to be taken
1) Toolkit from HPA/UKHCDO/SCIEH 1.1. Letter to clinicians 1.2. Panel recommendations 1.3. Clinical information 1.4. Patient letter (draft) 1.5. Patient information sheet 1.6. Exposure assessment form 2) List of all products ever implicated sent to clinicians from HPA/SCIEH. 3) Centre-specific batch information sent to Haemophilia Centre Directors, Haematologist or Blood Bank Manager from BPL or via other consignees	a) Inform patients ▪ all patients with bleeding disorders informed, advising on subgroup considered "at-risk". ▪ patients "at-risk" given opportunity to discuss/find out if received implicated batch and if so whether they have a high or low likelihood of being at potential additional risk of vCJD infection b) Complete exposure form ▪ place copy in patients notes ▪ send copy to UKHCDO ▪ (to be decided – mechanism for recording risk status in primary care record)

4.2 Primary immunodeficiency (PID) patients

At-risk: All patients who have been treated with VIGAM (intravenous immunoglobulin manufactured by BPL) beginning 1996 to end 2000 and assessed as having been exposed to a 1% or greater potential additional risk of infection.

Information provided to PID Immunologist (PIN)	Action to be taken
1) Toolkit from HPA/UKPIN 1.1. Letter to clinicians 1.2. Panel recommendations 1.3. Clinical information 1.4. Patient letter (draft) 1.5. Patient information sheet 1.6. Exposure assessment form 2) List of all products ever implicated sent to clinicians from HPA. 3) Centre-specific batch information sent to Blood Bank Manager or Principal Pharmacist from BPL	a) Confirm patients receiving VIGAM between 1996-2000 b) Inform patients ▪ all patients receiving VIGAM between 1996-2000 informed, advising that very few will be considered "at-risk", and giving opportunity to discuss. ▪ risk is being calculated and patients will be contacted. c) Assess which patients are "at- risk" ▪ identify which patients have received the implicated batches. ▪ complete the individual risk calculation using the exposure form. ▪ place copy of exposure form in patient's notes. ▪ (to be decided – mechanism for recording risk status in primary care record) ▪ forward copy of exposure form to HPA-CDSC. d) Inform 'at-risk' patients after consultation with current GP. e) Inform all patients not "at-risk" ▪ patients not "at-risk" given option of knowing whether or not they received implicated batches although the amount of potential vCJD infectivity is less than that required to be defined as 'at-risk' by the CJDIP.

4.3 Others affected

At-risk: All patients who have been treated with implicated products beginning 1987 to end 2001 and assessed as having been exposed to a 1% or greater potential additional risk of infection.

Information provided to Medical Directors of Trusts, NBS, Clinical Trials Coordinators	Action to be taken
1) Copy of letter and advanced notice of when going out to Angela Robinson/Pat Hewitt/Alan Slopecki 2) Toolkit from HPA to Trust Medical Directors sent via DH Gateway 2.1. Letter to clinicians* 2.2. Panel recommendations 2.3. Clinical information 2.5. Patient information sheet 2.6. Traceability questionnaire 2.7. Exposure assessment form * separate correspondence also sent to clinicians co-ordinating the clinical trial 3) List of all products ever implicated sent to clinicians from HPA. 4) Centre-specific batch information sent to Blood Bank Manager or Principal Pharmacist from BPL or via other consignees	a) Assess traceability of products ▪ focus on high/medium likelihood products. ▪ complete traceability questionnaire through liaison with the hospital pharmacy and/or blood bank, and the involvement of the relevant clinicians. ▪ send copy to HPA-CDSC. b) Where records are readily accessible and patients can be easily identified ▪ identify recipients of implicated batches ▪ complete the exposure form ▪ send copy to HPA-CDSC for risk assessment (Trusts will not be asked to do their own calculations) ▪ notify 'at-risk' patients (Trust responsible for clinical episode to make local arrangements in consultation with relevant general practitioners) c) Handling enquiries from former and current patients ▪ Reassure and say they will be contacted in due course by clinician providing their care if an exposure that warrants further action is traced back to them. ▪ for further information contact NHS Direct .

4.4 General public

Information provided to NHS Direct	Action to be taken
1. Panel recommendations 2. Management strategy 3. Who might be affected 4. Background information 5. Clinical information 6. Patient information sheet	a) Formulate key message ▪ Panel recommendations ▪ summary diagram of notification exercise ▪ who might be affected b) Respond to callers ▪ anybody who might be at higher risk is being followed up through clinicians. ▪ callers will be contacted in due course by their clinicians if an exposure that warrants further action is traced back to them. ▪ otherwise they should be reassured.
Information provided on HPA website 1. Summary text 2. Panel recommendations 3. Management strategy 4. Who may be affected 5. Background information 6. Clinical information 7. Patient information sheet	c) Further information for patients ▪ NHS Direct ▪ refer to HPA and other websites.

4.5 HPA

Information provided to Regional Co-ordinators/ HPUs/Regional Microbiologists/Regional Communications Officers via the Regional Director	Action to be taken
1. Letter for information* 2. Copy of all other documentation * refer to HPA website for further information	a) Letter to RDs from Deputy Director (Operations) HPA LARS ▪ informing them what is happening ▪ asking them to identify one person (regional coordinator) to cascade information to local HPUs b) Regional coordinators ▪ to cascade information to HPU leads, regional microbiologist (or equivalent) and regional communications officer ▪ to handle general queries by acting as 'filter' between region and HPA CJD Section c) Regional microbiologists to cascade information to local infection control teams d) HPU leads to cascade information to PCT directors of public health e) Regional communications officers to link with local comms teams (SHAs/PCTs) on local response, DH Comms for guidance.
Information provided internally at HPA-CDSC (Colindale) 1. Information for duty doctors	f) ensure triage ▪ duty doctors ▪ CJD website mailbox cjd@hpa.org.uk ▪ CJD Section contact numbers (direct) ▪ (Haemophilia Directors) ▪ (PIN Immunologists) ▪ (Medical Directors) ▪ (Clinical Trials) ▪ (NHS Direct) ▪ (Consignees)

4.6 Consignees

Information provided to Consignees (UK)	Action to be taken
1) General letter – centre-specific where received implicated batches 1.1 list ever-implicated batches (high/med/low - unstratified) 1.2 summary of situation in UK 1.3 clarify routes of communication 1.4 contact details 2) Panel recommendations 3) Panel tables 4) Summary diagram of notification exercise 5) General letter centre-specific where NOT received implicated batches **FOR BATCHES OF INTERMEDIATE** **a) ever-implicated intermediate** **b) summary of situation** **c) detailed risk assessment may be possible [advice offered by NHS users must be consistent with that given to other NHS users in the UK]** **c) HPA able to offer advice & will be contacting at later date to establish this**	a) Contact Haemophilia Centre Director, PID Immunologist, Medical Director (where not the consignee) to confirm centre-specific information. b) Relevant clinicians (above) have been asked to liaise with consignees in order to confirm which implicated batches were distributed to their centre/Trust. c) If clinicians have not received information from HPA, ask them to contact HPA CDSC. d) NBS to provide centre-specific information where acted as distributor
Information provided to Consignees (EU) 1) General letter – distributor specific 1.1 list ever-implicated batches (high/med/low – unstratified) (marked if samples) (marked if previously notified) 1.2 summary of situation in UK 1.3 HPA able to offer advise at request of MoH **FOR BATCHES OF INTERMEDIATE** **a) ever-implicated intermediate**	

b) summary of situation in UK
c) HPA able to offer advise at request of MoH

Information provided to consignees (Other Overseas)

1) General letter – distributor specific
1.1 newly implicated batches (marked if samples)
1.2 summary of situation in UK
1.3 HPA able to offer advice at request of MoH

FOR BATCHES OF INTERMEDIATE
a) newly implicated intermediate
b) summary of situation in UK
c) HPA able to offer advise at request of MoH

4.7 Other liaison

Information provided to:	Action to be taken
1) Haemophilia Society(Graham Whitehead) 2) PIA (David Watters) 3) Haemophilia Nurses Association (Vicky Vidler) 4) World Federation of Haemophilia (Brian O'Mahony) 5) British Federation of Haemophilia 6) CJD Support Network (Gillian Turner) 7) Human BSE Foundation (Frances Hall) 8) National CJD Surveillance Unit (James Ironside) 9) National Prion Clinic (John Collinge) 10) Cadre of Experts 11) CJD Incidents Panel 1. Letter for information* 2. Panel recommendations 3. Summary diagram of patient notification exercise 4. Who may be affected? 5. Clinical information 6. Patient information * refer to HPA website for further information	Send advance copy of information in confidence so can prepare own information including website text and links

5. List of Materials

Panel Recommendations
Annex to the Panel Recommendations (tables)
Clinical information
Patient information

Summary diagram of patient notification exercise
Background information
Who might be affected?

Letter to haemophilia centre director
Letter to PIN immunologist
Letter to HPA etc
Letter to Medical Director of Trust
Letter to Clinical Trial Co-ordinators
Letter to Other liaison

Letter to patients with bleeding disorders (draft)
Letter to PID patients (draft)

Patient vCJD exposure form – bleeding disorders
Patient vCJD exposure form – PID
Patient vCJD exposure form – others affected
Traceability questionnaire – others affected

Products Notification – UK Consignees
Products Notification – EU Consignees
Products Notification – Other Overseas Consignees
Products Notification – UK Distributors Intermediate Batches
Products Notification – EU Distributors Intermediate Batches
Products Notification – Other Overseas Intermediate Batches
Summary to accompany products notification UK
Summary to accompany products notification EU
Summary to accompany products notification Other overseas

6. PROJECT TIMELINES

Project Timelines

	M	T	W	T	F	S	S	M	T	W	T	F	S	S	M	T	W	ACTION
	..	..	n-13	..	..	..	..		..	n-6	..	..	..	..	n-1	n	n+..	
			11/08							18/08					23/08	**24/08**		
[1]Toolkit to UK Haemophilia Centre Directors			X															HPA/UKHCDO/SCIEH
Toolkit to UK PID Immunologists			X															HPA/UKPIN/SCIEH
Toolkit to Medical Directors of Trusts/NBS (England, Wales, NIreland)			X															HPA
Toolkit to NHS Direct			X															HPA
Toolkit to HPA RDs			X															HPA
UK Haemophilia Centre Directors prepare letters & information to patients			X	X	X			X	X	X	X	X						Clinicians
UK PID Immunologists prepare letters & information to patients			X	X	X			X	X	X	X	X						Clinicians
Information to other liaison groups										X								HPA
Information to Devolved Administrations										?								DH
Information to International Desk										?								DH
Letter & information to patients with bleeding disorders (all)															X			Clinicians
Letter & information to patients with PID (recipients of VIGAM 1996-2000)															X			Clinicians
Information to HPA-CDSC Colindale																X		HPA
BPL Notification of implicated batches to UK consignees																X		BPL
BPL Notification to EU consignees																X		BPL
BPL Notification to other Overseas consignees																X		BPL
List of implicated batches to clinicians from HPA																X		HPA
?DH Announcement & Press Release?																X		DH
HPA www-information																X		HPA
Clinicians complete exposure assessment form & appointments for patients begin																X	...	Clinicians

[1] excluding Annex to Panel recommendations (tabular lists of implicated batches): this information will be made available on the notification date (n=24/08)

6. PROJECT TIMELINES

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7. SUMMARY DIAGRAM OF PATIENT NOTIFICATION EXERCISE