

MANAGING NOTIFICATIONS OF ADVERSE REACTIONS TO FRACTIONATED BLOOD PRODUCTS

REASON FOR ISSUE: Change in wording under Key Responsibilities, 8.4.1 and 8.4.5 to fit with current practices and to clarify meaning. Change CSL to CSL Behring.

1. BACKGROUND

Fractionated blood products are medicines prepared from human blood by large scale pharmaceutical manufacturing processes. They do not include blood components that are normally manufactured in closed systems where sterility is maintained by aseptic handling methods.

Monitoring of adverse events that arise during or after administration of manufactured blood products is required to assist with understanding whether, and if, these events:

- Are associated with individual fractionated blood products, or batches of these products; (particular concern exists for detection of reactions to new or modified products.)
- Occur with a higher incidence in recipients with a particular clinical condition.
- Are more likely to occur as a result of the effects of another medicine or clinical treatment.

The term 'blood products' used without further qualification is used in this document to refer to blood components and fractionated blood products.

2. PURPOSE

Data on adverse reactions is collected at the request of Medsafe and for the purposes of NZ Blood Service, to both monitor the frequency and nature of adverse events and to provide an early warning system of adverse reactions to new or modified fractionated blood products. One of the NZBS purposes for collecting the data is to provide a mechanism for reporting adverse reactions to CSL Behring as part of a contractual relationship that is overseen by the Australian Therapeutic Goods Administration, or applicable global regulatory authority.

It is intended that the monitoring programme will result in timely advice from NZBS to the sponsor of the product of adverse reactions to a fractionated product, and where appropriate to Prescribers of the product.

Reports will be provided regularly to CARM.

3. SCOPE

Clinicians in New Zealand are requested to notify all adverse reactions arising from, or in association with the use of, blood products.

Notifications will be reported to, and collated by NZBS as the agent authorised in New Zealand to collect blood donations and to manufacture blood for therapeutic use. The reporting and monitoring process will cover products prepared from blood donations collected from New Zealand donors and other products imported either by NZBS or by commercial companies.

Some materials imported for in vivo diagnostic procedures contain human plasma proteins. Users of these products are encouraged to notify adverse reactions arising from these products using the NZBS notification process but it is recognised that NZBS is not in a position to monitor the importing or use of these products and cannot identify all Users of these products.

4. KEY RESPONSIBILITIES

- Transfusion Medicine Specialist at Collating Centre: Review of adverse events, manage relevant data at the Collating Centre and reporting to CSL Behring.

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- Transfusion Medicine Specialists throughout NZ: Review of adverse events in regions, supply of relevant data to the Collating Centre. Reporting to CSL Behring when required.
- Transfusion Nurse Specialists: Assist with collecting and reporting data to the Collating Centre. Assistance with reporting to CSL Behring may be required.
- Blood Bank Staff: Supply Notification Forms to clinical staff, assist Clinical Staff with completing form and relay completed form to Collating Centre.
- Secretary: Maintain record files, prepare and send reports.

5. DEFINITIONS

- 'Blood products' is a general term that refers to both blood components and fractionated blood products.
- CARM – Centre for Adverse Reactions Monitoring
- The Notifier – the person who reports the adverse event to NZBS or to a non-NZBS Blood Bank, or an NZBS Staff member who has identified the adverse event and reports it to the National Collating Centre.
- WAVES Number – the Case identification number allocated by CSL Behring Pharmacovigilance Staff.

6. ITEMS REQUIRED

6.1 Equipment

- Nil

7. DOCUMENTS

7.1 Required Documents

- 111F003 Notification of Adverse Reaction to a Fractionated Blood Product.
- 111F009 Notification and Investigation of Adverse Transfusion Reaction.
- Electronic folders and files:

National V:\ Clinical \ Adverse Events to Fractionated Products \ Folders:

- CSL Reports in Process
- CSL Reports Sent
- Master Reporting Files

File names:

- CSL Fax master
- CSL Fax update master
- Progress status for Follow up of Adverse Reaction
- Current Suspected ADR Report Form (CSL Behring controlled document)
- Current Pregnancy Outcome Form (CSL Behring controlled document)
- Questionnaire for Hepatitis ADE (CSL Behring controlled document)

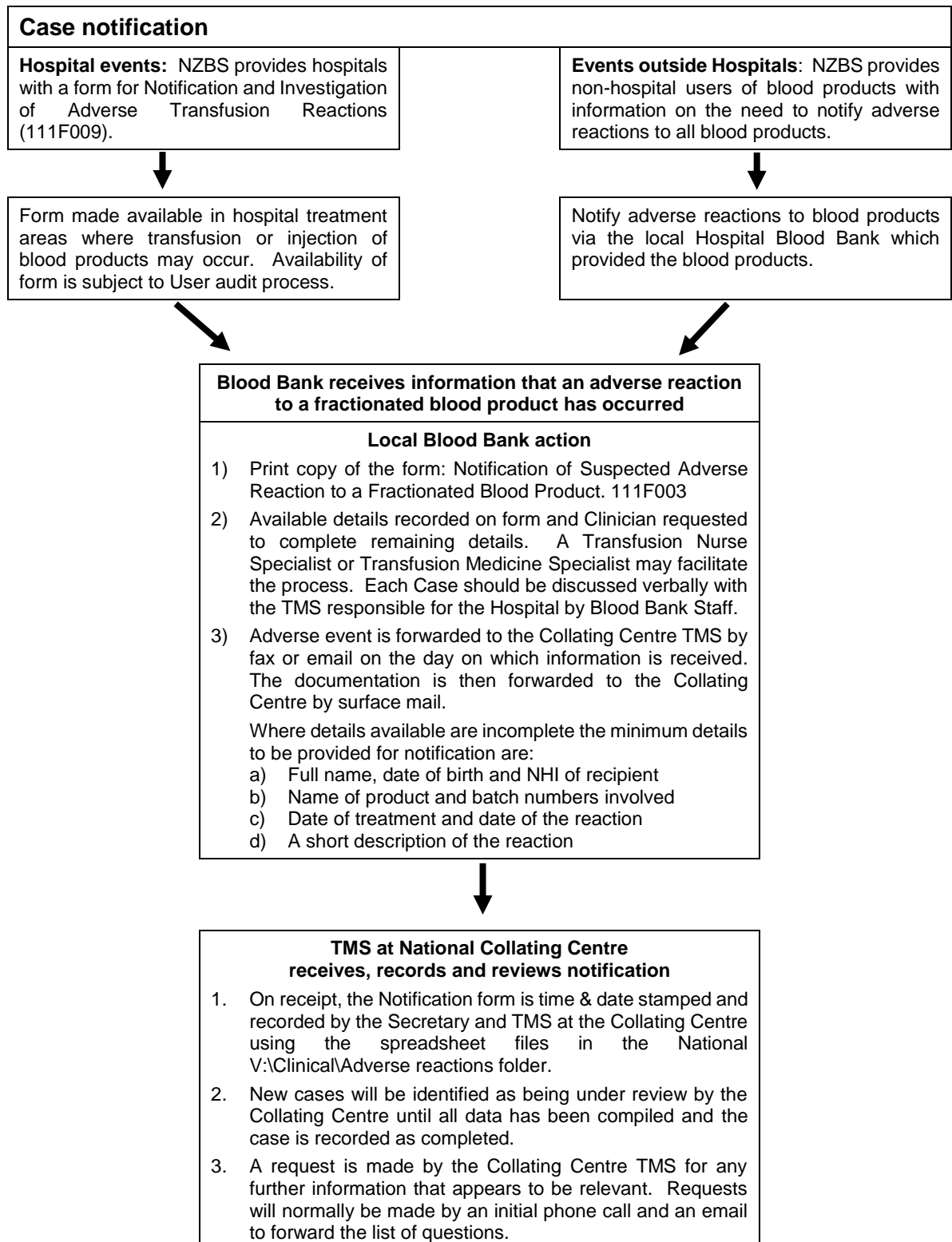
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7.2 Related Documents

- Nil

8. PROCEDURE

Schematic Outline



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4. The Collating Centre (TMS and secretary) will monitor the spreadsheet and follow up again where responses are not received within 2-4 weeks.
5. Further information is added to the spreadsheet database when received.



NZBS National Collating Centre: collates and reports data to CSL Behring, CAG and CARM

1. The Manufacturer is notified of the information available using the Manufacturer's form (if requested) or by faxing a copy of the notification form 111F003.
2. Notification is required within 3 working days of receipt by an NZBS site in the case of toll fractionated products and 2 days for Section 29 CSL Behring products.
3. The minimum dataset for notification of a case to CSL Pharmacovigilance comprises the recipient's initials, implicated product name and batch, the date of the event and a short description of the event. No other patient identifiers are provided.
4. The National Medical Director will be contacted promptly if immediate NZBS action appears appropriate or if a case raises unusual and serious concerns.
5. Advice may be provided to: the local TMS in the region where the adverse event occurred and to the Clinician managing the recipient.
6. CSL Behring writes to Clinicians who notify adverse events, with a letter of acknowledgement and thanks.
7. A report is provided to each CAG meeting of all new cases not previously notified. The report format generated from the database spreadsheet will be used.
8. A periodic report will be provided to CARM using the NZBS format for all new cases.
9. A special report will be provided to Medsafe where review suggests a serious problem may exist:
 - With a particular product or product batch,
 - For a particular group of recipients, or
 - For recipients of a blood product who may have an adverse interaction of the product with other treatment

8.1 Case Notification to Local Blood Bank

- 8.1.1 The clinical notification form for adverse reactions to all blood components and fractionated blood products is 111F009. It is provided in pads of 10 forms for use in hospital wards and other clinical areas where transfusion or administration of blood products may occur. Where a notification is received by other means, eg; telephone or a written note, this stage may be bypassed in the case of adverse reactions to fractionated blood products.

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- 8.1.2 Blood Bank Staff, or if involved, the Transfusion Nurse Specialist or Transfusion Medicine Specialist will print the form 111F003 (Notification of Suspected Adverse Reactions to Fractionated Products).
- 8.1.3 Data is transcribed from the notification form 111F009, or other source, onto the adverse reaction notification form and further data required to complete the form is obtained from the clinical staff concerned. The details may be obtained by requesting the clinical staff to complete the notification form, or verbally requesting specific items not already notified and completing the form in the Blood Bank. The primary record on 111F009 must be retained.
- 8.1.4 If not already informed, the TMS responsible for the Hospital/Region should be informed of each report. This process should not delay notification of the Collating Centre.

8.2 Local Blood Bank Actions

- 8.2.1 The completed form is forwarded to the Transfusion Medicine Specialist at the National Collating Centre by fax or email. This must occur within 24 hours of initial receipt of information about the adverse event by NZBS Staff.
- 8.2.2 In a case considered urgent by the Regional TMS or local Hospital Staff the Blood Bank Staff should contact the Collating Centre Staff by telephone immediately.
- 8.2.3 The Adverse Reaction Notification Form is then forwarded to the Collating Centre by mail together with any relevant clinical or laboratory documentation.

8.3 National Collating Centre Actions

- 8.3.1 On receipt the notification is date stamped, initialed and allocated the next adverse reaction event number from the main spreadsheet record.
- 8.3.2 The paper records for each case are held in a sequential numbered file. The sequence for items in each file record is: (front to back):
- Most recent NZBS CAG record
 - Most recent notification to CSL Behring / other manufacturer
 - Previous editions of NZBS CAG record and notifications to Manufacturer
 - Request(s) for further information about each case, responses and any other information related to the case
 - Original notification.
- 8.3.3 Electronic records are held in the folder: \ National V: \ Clinical \ Adverse events to fractionated products. The folder structure is used to hold master files supplied by CSL Behring, NZBS master files and current or work files. The main spreadsheet for holding data is backed up with a copy that has the suffix 'b' added to the title. The backup copy is to be updated at the end of each session.
- 8.3.4 The Secretary enters recipient demographic and Notifier data, together with any other basic data supplied. If the secretary is unavailable the TMS will enter all data.
- 8.3.5 The TMS reviews the data entered, enters all remaining data, reviews the event and identifies additional data needed to evaluate the event.

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- 8.3.6 The Follow-up request form located in the 'Patient data' folder is used as a template to request further information from the Notifier or other relevant person. An electronic version of the request is saved in the Patient data folder using the file naming convention: year_case number Surname Initials NHI date of record, e.g. 09_01 Bloggs J XXXnnnn 20090125.
- 8.3.7 The Notifier is contacted by telephone to briefly discuss the case and indicate that additional information is needed. The purpose of the call is to facilitate a prompt reply. The request should normally be sent by email or fax, or if these are not suitable, by mail.
- 8.3.8 Any telephone call dealing with a case will be documented, dated and signed using the form 'Telephone Call NZBS' located in the 'Patient data' folder. After recording of any new data in the spreadsheet and preparing any relevant notification for CSL Behring, the completed form is filed with the case documents. If completed electronically, the file should also be saved in the Patient data folder using the filename convention given in 8.3.6.
- 8.3.9 Manual recording by delegated TNS/TMS: When the TMS who collates data and reports to CSL Behring is unavailable, the role will be delegated to the local TNS or a TMS at another site. A fax coversheet will be made available to facilitate reporting to CSL Pharmacovigilance. Assistance from a TMS may be required to confirm clinical information and to identify further information that may be required.
- 8.3.10 In the case of serious or life-threatening adverse reactions CSL Behring will require prompt completion of all details in addition to the minimum data set.

8.4 Reporting to CSL Behring

- 8.4.1 Faxing or emailing a scanned or other electronic file copy of the initial report to CSL Behring should occur within 3 working days of receiving the notification for toll fractionated products and 2 working days for Section 29 CSL Behring products. All personal identifying data for the recipient, other than initials and date of birth are to be redacted or obscured.
- 8.4.2 A review of outstanding cases should occur at 2-4 week intervals and if considered appropriate a further phone or email enquiry made to facilitate a response to any outstanding enquiry.
- 8.4.3 On receipt of a response from CSL Behring the WAVES number, and a CARM reference number, is entered for each case.
- 8.4.4 Each email communication from CSL Behring dealing with a case is printed and held in the relevant file.
- 8.4.5 Manual reporting by a delegated TNS/TMS: The person to whom the task is delegated will fax the adverse event notification to CSL Pharmacovigilance using the coversheet supplied. Notification to CSL Behring by fax or email must be completed as specified in 8.4.1. A record of communications with CSL Behring will be provided to the Collating Centre. The minimum data set to be reported is:
- Initials and date of birth [full names and NHI are not communicated to CSL Behring.]
 - Name of product and batch number(s) involved
 - Date of treatment and date of the reaction

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- A short description of the reaction
- If any of the above are not present in the original notification the information should be obtained and added by NZBS Staff so that the notification time-line is met.
- Where an adverse reaction is classified as serious (life-threatening) all relevant information should be sought and forwarded to CSL Behring as a matter of urgency.

8.5 CAG Reports

- 8.5.1 The CAG Case report is prepared in the data spreadsheet by copying the work sheet 'CAG'. The copy is assigned the name: suffix of year_case number, eg 09_01.
- 8.5.2 The summary page that will be included in the CAG agenda papers prior to the case reports is updated. This requires a one-line addition of core details for each case. The TMS will add a descriptive comment in the final column.
- 8.5.3 Prior to each CAG meeting the PA to the National Medical Director is notified of the cases that require be printing and including in the CAG Agenda papers and a copy of the case summary forwarded.
- 8.5.4 The Director of CARM is notified by the TMS of the new cases after each CAG meeting.

8.6 Other Reports

- 8.6.1 The National Medical Director will be contacted promptly where review of any case creates concern over the nature of the adverse event or the circumstances of the use of the product, or review suggests a clinical problem may exist:
- a. with a particular product,
 - b. for a particular group of recipients, or
 - c. for recipients of a blood product who may have an adverse interaction of the product with other treatment.
- 8.6.2 A special report will be provided to Medsafe (and copied to CSL Behring) where review suggests a serious clinical problem may exist with a product or its use.

9. MINIMUM TRAINING REQUIREMENTS (FOR NZBS USE ONLY)

<input checked="" type="checkbox"/>	Complete Document Sign-Off Sheet (108F060). • Read specified sections: Sections: <i>(Section 4, 8.4.1 to 8.4.5)</i>
<input type="checkbox"/>	Complete Document Sign-Off Sheet (108F060). • Read and understand whole document
<input type="checkbox"/>	Complete Document Sign-Off Sheet (108F060). • Formal training required. Specify: <i>(enter details of formal training)</i>
<input type="checkbox"/>	Complete Training Module <i>(enter name of module)</i>
<input type="checkbox"/>	No training required. Specify reason: