



PHARMACEUTICAL INSPECTION CONVENTION
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

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PIC/S GMP GUIDE FOR BLOOD ESTABLISHMENTS

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Editor: PIC/S Secretariat
P.O. Box 5695
CH-1211 Geneva 11

e-mail: daniel.brunner@picscheme.org
web site: <http://www.picscheme.org>

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1. DOCUMENT HISTORY

Adoption by Committee	22 May 2001
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2. INTRODUCTION

- 2.1 Blood components are often used in life threatening situations of severely ill patients. Allied to this is a heightened public awareness and expectation of the quality and safety of these products. Therefore, high standards of quality and safety of blood components have to be assured. These high standards can only be achieved by applying the principles of GMP during the collection, preparation, storage, dispatch, quality control and quality assurance of these products.
- 2.2 However, the implementation of GMP by blood establishments as well as the inspection of blood establishments by Competent Health Authorities is relatively new in many countries. It was considered by the PIC/S Blood Circle that a comprehensive GMP guide for blood components was missing and that as a consequence the implementation of GMP as well as the harmonisation of inspections was impeded. Therefore, the PIC/S Blood Circle undertook in 1996 the task of drafting a specific GMP guide for blood establishments and blood components.
- 2.3 It is apparent that some countries licence blood establishments and blood components, while others do not. However, the principles of GMP should apply to all blood establishments and the blood components which they prepare. It is intended that guidelines already in place, or intended to be issued, by a Competent Health Authority, the European Commission, Council of Europe and WHO, would be used in conjunction with this GMP guide. This GMP for Blood Establishments intends only to provide guidance that is specific for blood establishments (including apheresis establishments) and blood components.

3. PURPOSE

The purpose of this document is to provide guidance for GMP-inspectors to use during inspections of blood establishments. However, the document does also give an insight into the thinking and concerns of inspectorates and so could provide some useful information for blood establishments relating to the collection, preparation, storage, dispatch, quality control and quality assurance of blood and blood components.

4. SCOPE

- 4.1 At the time of issue this document reflects the current state of the art. It is not intended be a barrier to technical innovation or the pursuit of excellence. However, applicable national legislation should always be referred to when determining the extent to which the provisions laid down in this document are binding. This document should be used for PIC/S related inspections.

- 4.2 This document applies to blood and apheresis establishments relating to the collection, preparation, storage, dispatch, quality control and quality assurance of human blood and blood components.
- 4.3 This document does not apply to human blood and plasma when collected and tested for the sole purpose and exclusive use as the starting material for the manufacture of medicinal products which are prepared industrially by public or private establishments.

5. QUALITY MANAGEMENT

General

- 5.1 Blood establishments should take all necessary measures to ensure that a quality system is implemented and maintained. Quality should be the responsibility of all persons involved in collecting blood and preparing blood components.
- 5.2 The quality system should involve all activities that determine the quality policy, objectives, and responsibilities and implement them by such measures as quality planning, quality control, quality assurance and quality improvement within the quality system.
- 5.3 There should be units within the blood establishment organisation which are independent of preparation and which fulfil quality assurance (QA) and quality control (QC) responsibilities. The quality assurance unit should be involved in all quality-related matters and review and approve all appropriate quality related documents.

Quality assurance

- 5.4 The quality assurance system should ensure that all critical procedures, such as the purchase of raw materials, starting materials, selection of donors, collection of blood, preparation of blood components, storage, laboratory testing, dispatch and associated quality control measures, are specified in appropriate instructions and are performed in accordance with the principles of GMP and comply with Competent Health Authority regulations. The system should be reviewed by management at regular intervals to verify the effectiveness of the system and introduce corrective measures if deemed necessary.

Corrective and preventive action

- 5.5 The corrective and preventive action system should ensure that existing product nonconformity or quality problems are corrected and that recurrence of the problem is prevented.
- 5.6 The blood establishment should have methods and procedures in place to input product or quality problems into the corrective and preventive action system. Quality data should be routinely analysed to identify product and quality problems that may require corrective action or to identify unfavourable trends that may require preventive action.

Change control

- 5.7 A formal change control system should be in place to evaluate and document all changes that may effect the collection, preparation, storage, dispatch, quality control and quality assurance of blood and blood components.
- 5.8 The potential impact of the proposed change on the quality of the blood component should be evaluated. Scientific judgement should determine what additional testing and validation studies are needed to justify a change in a validated process.

Self-inspection

- 5.9 A system for self-inspection should exist. Self-inspections should be performed under the responsibility of the quality assurance unit by qualified persons to verify compliance with the principles of GMP and regulatory requirements.
- 5.10 Self-inspection should comprise all parts of the operations, be performed regularly and be documented. Corrective actions should be documented and completed in a timely and effective manner.

6. PERSONNEL

- 6.1 The collection of blood and preparation of safe and efficacious blood components is dependent on the availability of sufficient and appropriately qualified and trained personnel.

General

- 6.2 There should be an adequate number of responsible personnel to manage blood collection, component preparation, quality assurance and quality control. The quality control and quality assurance units should be independent of preparation functions. There should be a medical officer available in the organisation.

Responsibilities

- 6.3 The responsibilities of each member of the personnel should be described. There should be an organisation chart showing the hierarchical structure of the blood establishment.

Training

- 6.4 Personnel should receive initial and continuous training to ensure that they have the skills to perform their assigned tasks. Records should be maintained to demonstrate compliance to training requirements. The effectiveness of the programmes should be regularly assessed.
- 6.5 Personnel should have relevant knowledge of basic transfusion medicine, microbiology, hygiene and GMP.
- 6.6 Personnel in key areas of responsibility such as the QA manager, the QC manager, the Preparation manager and the Medical Specialist, should have

appropriate qualifications and experience, and specific training to discharge their responsibilities. Delegation should only be given to appropriately qualified and authorised individuals who have been trained for the task. Delegation should be in written form.

Hygiene

- 6.7 Written hygiene instructions should be present in each department of the blood centre. Personnel should wear appropriate clothing.

7. PREMISES

- 7.1 Premises should be located, designed, constructed, utilised and maintained according to the intended activity. The planning and layout should be designed to permit operations to take place in a logical order corresponding to the sequence of operations. Premises should be designed to permit effective cleaning, sanitisation and maintenance and to minimise the risk of errors.

General

- 7.2 Each area should be designed to suit the particular operation and should be arranged in a logical sequence of workflow.
- 7.3 Each area of preparation and storage should be secured against the entry of unauthorised persons. Working areas should not be used as a passageway by personnel.

Production areas

- 7.4 The area for blood donors should be separated from all production areas. Blood collection should be performed in an area intended for this purpose.
- 7.5 There should be suitable donor interview facilities, so that the interviews can be carried out in private.
- 7.6 The blood collection area should be organised in such a way as to ensure the safety of the blood donors and the staff, and to avoid of errors in the collection procedure.
- 7.7 Premises for the preparation of blood components should be situated, equipped and ventilated in a suitable way and used entirely for this purpose.
- 7.8 Storage areas should provide adequate space and suitable lighting and should be arranged and equipped to allow dry, clean and orderly placement of stored material under monitored conditions.
- 7.9 Storage areas should provide for properly secure and segregated storage of different categories of products and materials.

- 7.10 Storage areas should provide for suitable and effective segregation of quarantined and released blood and blood components. There should be a separate area for rejected products and material.

Environmental Control

- 7.11 The preparation of blood components should be carried out in an appropriately controlled environment, separated from activities which are not compatible. The design of the area should permit efficient cleaning and should not contain features that are incompatible to the preparation function.
- 7.12 Access to temperature and pressure controlled areas should be restricted and controlled. Environmental monitoring should be performed to demonstrate that the appropriate classification is consistently achieved. Records of the monitoring should be maintained.

Storage conditions

- 7.13 The temperature and humidity (where appropriate) in storage areas for materials, blood and blood components should be appropriately controlled, monitored and checked to demonstrate compliance with specifications and equal distribution throughout the storage facility. The checks should be recorded.
- 7.14 There should be an alarm system in place, audible and/or visible, to indicate when the storage temperature is outside acceptable limits. This alarm system should also cover the time period out of working hours. Regular checks of the alarm system should be performed and recorded. There should be a written procedure describing the actions to be taken in response to alarms.

Mobile sites

- 7.15 Premises used for mobile donor sessions should be of sufficient size and design to allow proper operation, cleaning, sanitisation and maintenance.
- 7.16 When assessing the suitability of a mobile site, consideration should be given to areas such as ventilation, electrical supply, lighting, hand-washing facilities, reliable communication to the central site, donor interview facilities and blood storage.
- 7.17 The suitability of designated off-site premises should be assessed before operations commence.
- 7.18 Intermediate storage and transport of blood should be carried out under suitable temperature conditions to ensure that requirements are met.

8. EQUIPMENT

- 8.1 Equipment should be suitable for the intended use, should permit effective cleaning, sanitisation and maintenance and its technical standard should be suitable for the task. Instructions for use, maintenance, service, cleaning and sanitisation should be available and in the relevant language of the user.

General

- 8.2 Equipment for collection, preparation and storage of blood and blood components should be dedicated to its use.
- 8.3 New and repaired equipment should meet qualification requirements when installed and authorised before use. Qualification results should be documented.

Maintenance and calibration

- 8.4 Each item of equipment which could influence the quality of the blood or blood component should be regularly maintained and calibrated. Regular service should be performed and maintenance checks recorded.

9. DOCUMENTATION

- 9.1 The documentation of procedures and records is essential to a quality assurance system. It ensures that work performed is standardised, and that there is a traceability of all steps in the manufacturing of blood and blood components; i.e. donor selection, collection, preparation, storage, dispatch, quality control and quality assurance.

General

- 9.2 Each activity which affects the quality of the blood or blood component should be documented and recorded.
- 9.3 There should be a manual or computer system in place which ensures the traceability of the history of an individual blood donation or blood component from the donor to the finished product and vice versa, fully respecting confidentiality.
- 9.4 Records should be shown to be reliable and a true representation of the results. Records may be hand-written or transferred to another system, such as a computer or microfilm.
- 9.5 All records, including raw data, which are critical to safety and quality of the blood and blood components, should be kept in a secured storage area for at least ten years.
- 9.6 A document control procedure should be established to provide for review and a revision history of documents. It should include a distribution list.
- 9.7 All changes to documents should be acted upon promptly and should be reviewed, dated and signed by an authorised person.

Computers

- 9.8 The hardware and software of the computers should be checked regularly to ensure reliability. The software (program) should be validated before use.
- 9.9 Computer hardware and software should be protected against use by unauthorised persons. The users of computers should be trained and should be authorised only to handle data required for the task(s) they perform.
- 9.10 There should be documented procedures for backup protection against loss of records in the event of planned and unplanned function failures.
- 9.11 A procedure should define the routine action taken in the event of breakdown. Checks of these actions should be performed at least once a year.
- 9.12 Changes to computerised systems (hardware, software or communication) should be validated, applicable documentation revised (if appropriate) and personnel trained before the change is introduced into routine use. Only authorised persons should make changes to software.
- 9.13 Records of the changes to computerised systems (hardware, software or communications) should be retained for at least ten years.

10. DONOR SESSIONS

- 10.1 The selection of a suitable donor is the first important contribution to the quality and safety of blood and blood components. Selection criteria should ensure that the donor and the potential recipient are protected. Collection and handling techniques should ensure that the safety of the donor is not compromised.

General

- 10.2 For each important activity associated with the donation detailed records should be kept. The record should reflect also any unsuccessful donation, the rejection of a donor, adverse reactions or unexpected events.
- 10.3 The sterile blood bag systems used for the collection of blood and preparation of blood components should be approved by the Competent Health Authority unless (in the European Union) they are CE-marked. The certificate of analysis of each batch should be checked on receipt before use. The systems should be used in accordance with the instructions of the manufacturer.

Donor selection

- 10.4 Donors should be chosen using documented selection criteria and only volunteer donors in good health should be accepted.
- 10.5 The donor should be advised before donation of the requirements for blood donors and be informed of the common risks and discomforts associated with donating. Donors should be notified that the donation is tested for the presence of infectious disease markers and be informed of factors that may increase the risk to the recipient of donor blood. The informed consent form should be given to each donor and it must be signed off by the donor prior to collection.
- 10.6 The donor identification, donor selection interview and donor assessment should take place immediately before each donation.
- 10.7 The minimal criteria for donor selection should be determined by the Competent Health Authorities and should include essential indicators, as:
- the limits on the age of the donor;
 - the permissible frequency of donation;
 - the maximum volume collected at one donation;
 - the critical time intervals between donations;
 - the extent of the medical assessment;
 - the evaluation of the medical history, including history of infectious diseases (including regional epidemiology);
 - the factors in history and behaviour which may increase infection risk;
 - the reason for temporary deferral, including the length of time before donor acceptance is agreed;
 - the reason for permanent exclusion from further donation; and
 - the type of medication being used.
- 10.8 The criteria for an apheresis donor should meet at least the general acceptance criteria for blood donation, unless otherwise specified.
- 10.9 The criteria for autologous donor assessment should be determined by the Competent Health Authority.
- 10.10 All aspects of the donor assessment which are relevant to donor suitability should be recorded. The donor selection records and final assessment should be signed by an authorised interviewer.
- 10.11 A system of donation numbers should be used for the identification of each donor and donation and the linking of one to the other. The donation number should be traceable to all records linked to the donation.
- 10.12 For blood donations, laboratory samples should be taken at the time of donation. Procedures should be designed to avoid any risk of microbial contamination of

the unit as well as mix-up of samples. Laboratory samples awaiting testing should be stored at an appropriate temperature.

- 10.13 There should be procedures for each type of blood collection equipment, detailing the action to be taken when e.g. the flow rate is low or a power failure occurs.

Whole blood collection

- 10.14 The arrangement of the collection room should ensure that blood is collected in a safe and clean environment. Blood collection procedures should be designed to minimise the risk of microbial contamination.
- 10.15 The blood collection area should be designed and organised to minimise errors. Consideration should be given to the arrangement of donor beds and the handling of bags, samples and labels. Sterile blood collection and processing systems should be used for blood and blood component collection. A check should be made before use, to ensure that the collection system used is not damaged or contaminated, and that it is appropriate for the intended collection.
- 10.16 There should be a system in place to ensure that each donation can be traced to the batch of collection and processing systems into which it was collected and/or processed.
- 10.17 The venepuncture site should be prepared using a defined and effective disinfection procedure.
- 10.18 The donor should be re-identified immediately prior to venepuncture.
- 10.19 If a second venepuncture is required, a new venepuncture site should be used as well as a new blood collection system unless any contamination of the original blood collection system can be avoided.
- 10.20 Where an anticoagulant solution is used in the collection, the collection bag should be mixed gently immediately after start of collection and at regular intervals thereafter during the whole collection period.
- 10.21 The blood flow should not be interrupted for a significant time period during blood collection. The maximum collection time to accept the donation for component preparation should be specified and controlled. Donations which exceed the maximum time period should be recorded and not be used for component preparation.
- 10.22 The integral blood bag collection tubing should be sealed off at the end and then filled with anticoagulated blood as soon as possible after blood collection or sealed off as close as possible to the blood bag and then removed.
- 10.23 The procedure used for the labelling of records, blood bags and laboratory samples with donation numbers should be designed to avoid any risk of identification error and mix-up. At completion of the donation, the donation numbers issued should be checked on all records, blood bags and laboratory

samples. Donation number labels which have not been used should be discarded via a controlled procedure.

- 10.24 After blood collection, the blood bags should be handled at a storage temperature appropriate to further manufacturing requirements.

Collection by apheresis

- 10.25 Blood component collection by apheresis should meet the general criteria for blood collection, unless otherwise regulated by the Competent Health Authority.
- 10.26 The maximum extracorporeal blood volume of the apheresis procedure should be specified and not exceeded.

11. COMPONENT PREPARATION

- 11.1 The starting materials for blood component preparation are blood donations collected from suitable donors. The quality of these components is assured by control of all stages of production, including identification, labelling, storage conditions, packaging and dispatch.

General

- 11.2 The procedures should detail the specifications for materials which will influence the quality of the final blood product. In particular, specifications should be in place for blood and blood components (intermediate and final products), starting material, additive solutions, primary package material (bags) and equipment.

Starting material

- 11.3 Blood from donor sessions should be transported to the processing site under temperature conditions appropriate for the component which will be prepared.
- 11.4 There should be validation data to demonstrate that the method of transport maintains the blood within the specified temperature range throughout the period of transportation.

Preparation of Components

- 11.5 Blood and blood components should be placed in controlled and validated storage conditions as soon as practicable after venepuncture. The timing and method of separation is dependent on the blood component to be prepared.
- 11.6 The premises used for the preparation of blood components in a closed-system should be kept in a clean and hygienic condition and the microbial contamination load on critical equipment, surfaces and the environment of the preparation areas should be monitored. (As closed-system processing involves the use of pre-configured multiple bag systems, the only breach of the integrity of the system is during the act of blood collection and does not require to be carried out in a classified clean room).

- 11.7 The premises used for the production of blood components in an “open process” should preferably be a grade A environment with a grade B background, as defined in the current European Guide to Good Manufacturing Practice, Annex 1. A less stringent environment may be acceptable if in combination with additional safety measures such as preparing the blood component just in time for transfusion or immediately after preparation applying storage conditions which are unfavourable to microbial growth. Personnel performing open processing should wear appropriate clothing and should receive regular training in aseptic manipulations. Aseptic processing must be validated. (‘Open’ processing involves a breach of the integrity of the ‘closed system’, and as a consequence, a risk of microbial contamination).
- 11.8 Sterile connecting devices should be used in accordance with a validated procedure. The resulting weld should be checked for satisfactory alignment and the integrity validated. (The use of sterile connecting devices can be regarded as closed-system processing).
- 11.9 Before final release, a reconciliation procedure should be followed to ensure that all components of a donation are accounted for.

Irradiated Components

- 11.10 Regular dose-mapping of irradiation equipment should be performed. The exposure time should be set to ensure that all blood and blood components receive the specified recommended minimum dose, with no part receiving more than the maximum recommended dose. (The commonly recommended dose is not less than 25Gy and not more than 40Gy at any position within the unit). In case of a Cobalt source, allowance should be made at least annually for source decay and a second independent timing device should be used to monitor exposure time.
- 11.11 Radiation indicators should be used as an aid to differentiating irradiated from non-irradiated blood and blood components. A defined procedure should ensure the segregation of components which have not been irradiated from those which have been irradiated.

Labelling

- 11.12 The collected blood and intermediate and finished blood components should be labelled with relevant information of their identity and release status. The type of label to be used as well as the labelling methodology should be established in written procedures.
- 11.13 The label for a finished blood component should comply with the requirements by the ISBT 128 labelling system or contain at least the following information:
- the unique donation number; there should be traceability through the use of this number to the donor and all records of the manufacturing steps to the final product;
 - the product name;
 - the required storage conditions;

- the expiry date and, where appropriate, time;
- the date of collection of the donation(s) from which the blood component was prepared and/or the production date and time (where appropriate);
- the ABO and RhD blood group (where appropriate); and
- the name or other identification of the component preparation site.

11.14 The blood establishment responsible for the preparation of the blood component should supply the person(s) using the blood component with information on its use, composition, and special conditions which do not appear on the label.

11.15 For autologous blood products, the label should contain also the name and unique identification of the patient as well as the statement "Autologous Donation".

Release of products

11.16 Each blood centre should be able to demonstrate that a blood or blood component has been formally approved for release. Only an authorised person may release blood or blood components.

11.17 There should be a system of quarantine for blood and blood components to ensure that they cannot be released until all mandatory requirements have been satisfied. There should be a standard operating procedure which details the circumstances under which blood or a blood component can be released.

11.18 Before release, products should be kept in administrative and physical quarantine to prevent them from being dispatched. In the absence of a computerised system for product status control the label of a blood product should identify the product status and should clearly distinguish released from non-released (quarantined) product.

11.19 Records should demonstrate that before a component is released, all current declaration forms, relevant medical records and test results have been verified by an authorised person. If a computer is used to release results from the laboratory, an audit trail should indicate who was responsible for their release.

11.20 Where release is subject to computer-derived information the following points should be checked:

- the computer system should be validated to be fully secure against the possibility of blood and blood components which do not fulfil all test or donor selecting criteria, being released;
- the manual entry of critical data, such as laboratory test results, should require independent verification and release by a second authorised person;
- there should be a hierarchy of permitted access to enter, amend, read or print data. Methods of preventing unauthorised entry should be available, such as personal identity codes or passwords which are changed on a regular basis; and

- the computer system should block the release of all blood or blood components considered not acceptable for release. There should also be a means to block the release of any future donation from a donor.
- 11.21 Before they are destroyed, blood and blood components not acceptable for release should be quarantined in a secured storage facility.
- 11.22 Before final product release, if blood or blood component(s) have been prepared from a donor who has donated on previous occasions, a comparison with previous records should be made to give assurance that current records accurately reflect the donor history.
- 11.23 In the event that the final product fails release, a check should be made to ensure that other components from the same donation and components prepared from previous donations given by such donors have been identified. There should be an immediate update of the donor record to ensure that the donor cannot make a further donation, if appropriate.

12. STORAGE AND DISPATCH

- 12.1 Storage and dispatch routines should take place in a safe and controlled way in order to assure product quality during the whole storage period and to avoid mix-ups of blood products.

Storage

- 12.2 Procedures should detail the receipt, handling and storage of material and blood components.
- 12.3 There should be a system in place to maintain and control the storage of blood components during their shelf life, including any transportation that may be required.
- 12.4 Autologous blood and blood components should be stored separately.
- 12.5 Storage areas for blood components to be dispatched should be located near an entrance or exit to facilitate dispatch and to limit the numbers of personnel entering the main working areas.
- 12.6 Only authorised persons should have access to storage areas.

Dispatch

- 12.7 Prior to their dispatch, blood components should be visually inspected.
- 12.8 Dispatch of blood components should be made by authorised personnel. There should be a record identifying the person dispatching and the person receiving the components.
- 12.9 At the time of dispatch, there should be a procedure in place to ensure that all blood components to be issued have been formally released for use.

- 12.10 Packaging should be of a sturdy construction so as to resist damage and to maintain acceptable storage conditions for the blood and blood components during transportation.
- 12.11 The transportation and storage conditions for blood components, the packaging format and the responsibilities of the persons involved, should be in accordance with procedures agreed between the sites in question.
- 12.12 Once delivered, blood components should not be returned for subsequent dispatch. If blood components are returned on a routine basis, the following steps should be taken:
- the procedure for return of a blood component should be regulated by contract;
 - each returned blood component should be accompanied by a signed and dated statement that the agreed storage conditions have been met;
 - at least one sealed segment of integral donor tubing should have remained attached to the container; and
 - the records should indicate that the blood component has been re-issued and inspected before re-issue.

13. QUALITY MONITORING

- 13.1 There should be data validating each process in the preparation of blood and blood components, to ensure that they meet specifications. There should also be quality control data demonstrating that the process is under control.

General

- 13.2 All blood and blood components should comply with any specifications and test methods established by the relevant Competent Health Authority. All critical processes for blood and blood components should be validated. There should be quality control data demonstrating that the processes are under control.

Quality monitoring

- 13.3 Quality control of blood and blood components should be carried out according to a defined sampling plan. Where applicable, the practice of pooling of samples before testing should be clearly stated and the donations used in the pooled sample recorded.
- 13.4 Pooling of samples, such as for the measurement of FVIII in plasma, is only acceptable where comparative data of pooled samples and individual samples have demonstrated assurance of equivalence.
- 13.5 The sampling plan for testing of blood or blood components should take into account that most components are derived from an individual single donor, and should be considered as a single "batch".
- 13.6 A unit of blood or a blood component should not be released for use if it is tested by any method that compromises the integrity of the product.
- 13.7 The results of quality control testing should be subject to periodic review.

Microbiological contamination monitoring

- 13.8 Blood and blood components should be monitored for microbiological contamination according to specifications determined by the Competent Health Authorities to ensure both the continuing reliability of the established process and the safety of the final product. The sampling plan per product should take into account the type of system ('open' versus 'closed') that is used for the preparation of that blood component.
- 13.9 Where contamination is demonstrated, records should show action taken to identify the contaminant and the possible source.

Specifications of blood and blood components

- 13.10 There should be a system in place to ensure that specifications for processing and handling of blood and blood components are met.
- 13.11 Acceptance criteria should be based on a defined set of specifications for each blood and blood component.

14. LABORATORY TESTING

- 14.1 The testing of donors for infectious agents is a key factor in ensuring that the risk of disease transmission is minimised and that the blood components are suitable for their intended purpose.

General

- 14.2 All blood and blood components should be tested to ensure that they meet specifications and to ensure a high level of safety to the recipient.

- 14.3 Testing should be made on samples taken either at the time of collection or from sealed segments of integral tubing attached to the product container.
- 14.4 Testing of donation samples should be performed in accordance with recommendations of the test kit manufacturer.
- 14.5 Where applicable, testing of donation samples using “in-house” protocols should be validated.
- 14.6 There should be data confirming the suitability of any laboratory reagents used in the testing of donor samples and blood component samples.
- 14.7 The work record should identify the test(s) employed so as to ensure that entries, such as the calculation of results, are available for review.
- 14.8 Laboratory test results which do not satisfy the specified acceptance criteria, (those which are “reactive”), should be clearly identified, to ensure that blood and blood components of that donation remain in quarantine and the relevant samples are held for further testing.
- 14.9 The quality of the laboratory testing should be regularly assessed by the participation in a formal system of proficiency testing, such as an external quality assurance program.

Screening tests for infectious screening markers

- 14.40 Blood donors should be tested at each donation for antibodies to HIV-1/HIV-2, for antibodies to HCV, and for HBsAg.
- 14.11 Blood and blood components should be tested for other infectious agents or markers as required by the Competent Health Authority. The list should be regularly reassessed according to new knowledge, changes in disease prevalence in the population and the availability of new tests for serological markers.
- 14.12 Where blood and blood components have had a single reactive screening test, the original sample should be retested in duplicate according to the Competent Health Authority requirements.
- 14.13 Blood and blood components tested repeatedly reactive in any of the standard infection serology screening tests, i.e. anti-HIV, HBsAg, or anti-HCV, should be excluded from therapeutic use. They should be labelled as reactive and stored separately or destroyed.
- 14.14 The acceptance and rejection criteria for test results should be detailed in a procedure.
- 14.15 Samples to allow retesting should be retained from each donation, in the frozen state, for at least 2 years after collection.

Blood Group Serology Testing

- 14.16 All first time donors should be tested for ABO and RhD blood groups and (if applicable) clinically significant irregular red cell antibodies. Also donors with a history of transfusions or pregnancy since the last donation should be tested for clinically significant irregular red cell antibodies. Where applicable, the blood or blood component should be appropriately labelled.
- 14.17 The ABO and RhD blood groups of first time donors as well as repeat and regular donors should be tested according to the requirements set by the Competent Health Authorities.
- 14.18 If the ABO and RhD blood group is verified on a subsequent donation, a comparison should be made of the historically determined blood group. If a discrepancy is found, the applicable blood components should not be released until the discrepancy is unequivocally resolved.

15. COMPLAINTS AND RECALLS

- 15.1 To protect patients from defective blood products, each complaint concerning a component should be taken seriously and where appropriate, necessary measures should be taken.
- 15.2 Complaints and information on defective blood components should be documented and investigated within an appropriate time frame.
- 15.3 There should be a person(s) within the blood centre nominated to assess the need for blood component recall and to initiate and co-ordinate the necessary actions.
- 15.4 An effective recall procedure should be in place, ensuring prompt action at any time. The procedure should specify the responsibilities and actions to be taken in anticipated contingencies. Action should be taken within a reasonable time frame and should include traceability of all relevant supplied blood components and products and where applicable, should include look-back procedures.
- 15.5 The Competent Health Authorities should be notified of any recall or serious complaint of blood or blood components.
- 15.6 Any recall or serious complaint should be recorded and be followed by a thorough investigation of causative factors of the defect and, where necessary, the implementation of corrective actions to prevent recurrence.

16. REFERENCES

- WHO: Requirements for collection, processing and quality control of blood components and plasma derivatives. *Requirements for Biological Substances No. 27, revised 1992*
- Commission of the European Communities: Good manufacturing practice for medicinal products in the European Community. The rules governing medicinal products in the European Community, Volume IV, 1997
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- Council recommendation on the suitability of blood and plasma donors and the screening of donated blood in the European Community, 29 June 1998 (98/463/EC)
- ISO 9000:2000: Quality management systems – Fundamentals and vocabulary, current version
- PIC/S: Aide Memoire for Inspection of Blood Donation and Plasmapheresis Centres, 13 December 1996 (PS/W 5/96)
- United States Food and Drug Administration, Code of Federal Regulations, 21 Parts 600 - 799, revised as of April 1, 1997

17. RELEVANT TERMINOLOGY

Apheresis	Process by which one or more blood components is selectively obtained from a donor by withdrawing whole blood, separating it by centrifugation or filtration into its components, and returning those not required to the donor.
Blood (Whole blood)	Whole blood collected from a single donor and processed either for transfusion or further manufacturing.
Blood component	Therapeutic components of blood (red cells, white cells, plasma, platelets) that can be prepared by centrifugation, filtration, and freezing using conventional blood bank methodology.
Blood establishment	Any enterprise or body that is involved in any aspect of the collection and testing of human blood or blood components, whatever their intended purpose, and their processing, storage and distribution when intended for transfusion.

Blood product	Any therapeutic product derived from human blood or plasma. Encompasses both labile blood components and stable plasma and cell derivatives.
Closed system	System developed for the aseptic collection and separation of blood and blood components, manufactured under clean conditions, sealed to the external environment and sterilised by an approved method.
Donor	A person in normal health with a good medical history who voluntarily gives blood or plasma for therapeutic use.
First time donor	Someone who has never donated either blood or plasma
GMP	Good Manufacturing Practice: All elements in the established practice that will collectively lead to final products or services that consistently meet appropriate specifications and compliance with national and international regulations.
Manufacture	All operations of purchase of materials and products, Production, Quality Control, release, storage, dispatch of blood components and the related controls.
Mobile site	Blood collection unit operated off-site from a permanent collection site.
Open system	System in which a breach has occurred but every effort is made to prevent microbial contamination by operating in a clean environment using sterilised materials and aseptic handling techniques.
Preparation	All operations from the receipt of blood or blood component (after its collection) to its completion as a finished blood component.
Procedure	Description of the operations to be carried out, the precautions to be taken and measures to be applied directly or indirectly related to the manufacture of a blood product.
Product release	Process which enables a product to be released from a quarantine status by the use of systems and procedures to ensure that the finished product meets its release specification.

Production	All operations involved in the preparation of blood components, from the collection of blood or blood component, through processing to its completion as a finished blood component.
Quality	Totality of characteristics of an entity that bear on its ability to satisfy stated and implied needs. Consistent and reliable performance of services or products in conformity with specified standards.
Quality assurance	All planned and systematic activities implemented within the quality system and demonstrated as needed to provide adequate confidence that an entity will fulfil requirements for quality.
Quality control	Operational techniques and activities that are used to fulfil requirements for quality in compliance with the specification.
Quality management	All activities of the overall management function that determine the quality policy, objectives, and responsibilities and implement them by such means as quality planning, quality control, quality assurance, and quality improvement within the quality system.
Quality monitoring	That part of a quality assurance programme concerned with maintenance and improvement of quality which deals with the identification and use of indicators to detect variations from standards or specifications.
Reconciliation	Comparison and assessment of any discrepancy between the amount of material entering and leaving a given operation or series of operations.
Regular donor	Someone who routinely donates their blood or plasma (i.e. within the last two years), in accordance with minimum time intervals, in the same donation centre.
Repeat donor	Someone who has donated before but not within the last two years in the same donation centre.
Responsible personnel	Individuals with relevant qualifications and experience for the scope of activities carried out in a blood establishment.
Self-inspection	An audit carried out by people from within the organisation to ensure compliance with GMP and regulatory requirements.
Sterile Connecting Device	A device that connects two tubes without breaching the sterility of their interior.

Validation

That part of a quality assurance system that evaluates in advance the steps involved in operational procedures or product preparation to ensure quality, effectiveness, and reliability.

18. REVISION HISTORY

Date	Version Number	Reasons for revision
1 July 2004	PE 005-2	Change in the Editor's co-ordinates
