Standards and Guidelines For Blood Transfusion Services

Ministry of Health
Government of Pakistan

Blood Transfusion Services of Pakistan
STANDARDS and GUIDELINES for BLOOD TRANSFUSION SERVICES

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PREFACE

This first edition of Standards and Guidelines for Blood Transfusion Services (BTS) sets out the practical norms vis-a-vis the existing clinical practices and available infrastructure. According to the current estimates approximately 1.5 million blood bags are annually transfused in Pakistan with a ratio of 60:40 between private and public sectors. The federative units in Pakistan i.e. Provinces and Areas have the administrative control and responsibility for logistic support of their respective Blood Transfusion Services (BTS). The present scenario for BTS appears to be rather fragmented and without requisite support. An administrative structure of BTS exists only in Punjab Health Department and such systems however would hopefully be initiated in other Provinces.

The workshops assisted by World Health Organization on various aspects of transfusion medicine are being regularly conducted since 1994 under the auspices of the Ministry of Health/National AIDS Programme, NIH and the Provincial Departments of Health. There has been a burgeoning desire by the participants of these activities representing both public and private sectors and NGOs that Pakistan should have uniform Guidelines and Standards for Transfusion Medicine. The legislation bills for the safety of Blood Transfusion at federal and provincial levels are in the process of approval while it has been already passed in Sindh. Soon after the approval and enactment of these bill(s), Standards for private and public sector blood banks will be required and therefore should be ready well in time.

A number of WHO documents and Guidelines adopted by other member states countries were reviewed and consulted for this purpose. Major portion of these standards has however been adopted from the "Guidelines for BTS in the UK". The participants of the above mentioned national workshops actively contributed to develop the framework documents to formulate the Guidelines for the clinical use of blood and blood products in Pakistan. Existing practices, attitudes and professional background of the users and available infrastructure(s) at various levels in the country were considered during consultative meetings while developing these guidelines.

This is, however only a first step and a lot more remains to be produced on the issues like quality management including GMP/GLP, quality control, national proficiency testing exercises, hospital Blood Transfusion Committees and Clinical audit etc. The revision of this first edition will continue in future through Working Groups, Task force and the proposed Provincial Blood Transfusion Authorities and National Blood Transfusion Committee. The suggestions, guidance and critique from the working specialists and medical profession is welcome since it is the main tool to enhance the quality of this manuscript in the years to come.

Lt. Gen ® Mohammad Saleem
Executive Director & National Coordinator
Acknowledgements

The completion of this work brings a happy moment. It also provides a welcome opportunity to acknowledge deeply felt debt of obligation for a very kind soul, an authority, Dr. Freydoun A. Ala on behalf of the whole team which participated in formulation of this manuscript. Most valuable professional guidance and expertise remained available to us through Lt. General Mohammad Saleem, the Executive Director of NIH who himself is the senior most haematologist in this country.

The programme managers of BTS in Punjab (Professor Aquela Bhutta and Dr. Mefooz ur Rehman), Sindh (Dr. Altaf Shaikh), NWFP (Dr. Fazale-Razik), Balochistan (Dr. Nadeem Samad), AJK (Dr. Mohammad Sadiq) and Northern Areas (Dr. Abdul Latif) took part in compilation of these guidelines most dedicatedly. Their valuable efforts need to be acknowledged gratefully.

Senior members of Pakistan society of Haematology, more especially Professor Mueen-ud-Din (Baqai Medical College, Karachi), Professor Abdul Hayee (Shaikh Zaid Hospital, Lahore), Professor Khalid Zaffar Hashmi (Liaqat National Hospital, Karachi), Professor Abdul Khaliq (Ayub Medical College, Abbottabad), Brigadier Zahoor ur Rehman (Armed Forces Institute of Pathology, Rawalpindi) and Colonel Farook Khattak (Armed Forces Institute of Transfusion, Rawalpindi) gave very useful suggestions and critique which unmistakably provided us solid grounds for completion of this task.

The officers and staff of the National AIDS Programme gave immense inputs which really are beyond measure. More especially, Dr. Hamayun Asghar (Virology Department), Dr. Muhammad Salman, Dr. Asma Bokhari, Dr. Altaf H. Bosan, Mr. Sajid Husain Shah, Mr. Muhammad Qasim Janjua, Mr. Gulfranz Khan and Mr. Ashfaque Khan devoted their personnel time willingly, which is a commendable effort on their part.

WHO/EMRO has always taken a keen interest for the betterment of Blood Transfusion Services in Pakistan and for development of these National Standard Guidelines. Dr. Mohammad Ali Barzgar, WHO representative in Pakistan took personal interest, provided guidance and gave valuable suggestions virtually in every hour of crisis. All the officers and staff of the WHO office, Islamabad were always willing to help and resolve problems.

Most importantly, this was a persistent desire and continuous encouragement from the Federal Secretary and the Director General Health without which the formulation of these Guidelines would have never been possible. They deserve an enduring gratitude for their support, patronage and guidance. May the Almighty bless every one who took part in this effort.

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SECTION 1

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Chapter 1

Selection of Donors

1.1 General Considerations

1.1.1 Donations of whole blood or some of its components provide the material from which all blood products are derived. The criteria for selection of blood donors apply equally to donors of whole blood and of cellular or plasma components collected by aphaeresis.

1.1.2 The selection of suitable blood donors have the purpose of ensuring that the potential donor is in good health for two reasons.

1. To protect the recipient from any ill-effect through transmission of disease or drug by blood transfusion.

2. To protect the volunteer donor from any harm.

1.1.3 Only persons in good health should be accepted as donors of blood for therapeutic use.

1. The prospective donor's medical history should be evaluated on the day of donation by a suitably qualified person who has been trained to utilize accepted guidelines for the selection of blood donors.

2. If there is any doubt about the suitability of a prospective donor, a donation should not be taken and the details should be referred to a medical practitioner for a decision.

3. Each organization responsible for the collection of blood should include a medical consultant ("consultant in charge of donor care") who will take ultimate responsibility for the selection and care of donors. The immediate responsibility is that of the medical practitioner or senior nurse in attendance at the session.

1.1.4 Donors with Hazardous Occupations or Hobbies

1. Service aircrew, whether trained or under training are not permitted to act as blood donors. Civil aircrew may not donate if on flying duties.

2. Occupations where a delayed faint may present a hazard either to the donor or to others accept only when the individual is going off duty, e.g. train, HGV or bus driver, heavy machine or crane operator, driver, climbing ladders or scaffolding, miner working underground.

3. "Hazardous" hobbies should not be followed on the day of donation, e.g. gliding, powered flying, car or motor cycle racing, climbing, diving etc.
1.1.5 Patients referred for therapeutic venesection should not be accepted at donation sessions.

1.1.6 The Guidelines in this Chapter do not apply to donor (people) wishing to give blood for autologous transfusion. Specific guidance for autologous transfusion is given in Transfusion Medicine, 1993,3,307-316.

1.2 Medical Assessment

1.2.1 Each donor must undergo an assessment to determine eligibility to donate. A significant part of the assessment procedure will usually rely on answers to simple standard questions relating to general health, past medical history and medication. This is combined with simple visual assessment of the donor and selected testing of samples collected at the time of donation.

1.2.2 In order to obtain relevant information about medical history, a standard set of questions must be put to each prospective donor. The eligibility should be determined by reference to a comprehensive listing of donor selection criteria. The relevant Blood Transfusion Authorities will produce guidelines and necessary documents regarding medical assessment of donors at federal and provincial levels.

1.2.3 All blood collection sessions should have facilities, which provide for privacy and confidentiality for any donor, wishing to discuss potentially sensitive issues. Donors must be reassured about the confidentiality of such information provided.

1.2.4 Potential donors who are blind, partially sighted or illiterate should be informed of the contents of the literature and the notices regarding testing of donations.

1.2.5 Age

1. Donors should generally be between the age of 18 and 65 i.e. from their eighteenth to sixty-sixth birthday. It is general practice to set an upper age limit of 60 for first time donors in view of the increased incidence of cardiovascular disease over that age and potential adverse effects in first time donors.

2. Donors may be accepted, subject to national policy, from the age of 17 years.

3. The Consultant in charge of donor care may authorize continuation of donation beyond the age of 65, up to the donor's seventieth birthday, but in these cases due regard should be made of the increased likelihood of coincident events which might be precipitated by or associated with the act of blood donation.

1.2.6 Frequency of donations

An interval of 16 weeks between donations of whole blood is considered a reasonable frequency. An interval of 12 weeks is an absolute minimum.

1.2.7 Volume of donation
No more than 13% of the estimated blood volume should be taken during one blood donation. For an individual weighing over 50 Kg (7 stone 12lbs), a donation of 450 ml is usually taken.

1.3 **Medical history of donors**

1.3.1 General considerations

1. All volunteer donors should clearly understand any information and/or questionnaire presented to them. Any condition declared should be discussed with the medical practitioner or suitably trained staff in attendance at the blood collection session unless clear, unequivocal instructions regarding the responses are available to the member of staff conducting the questioning.

2. Donors whose serum or plasma or cells are to be used for laboratory, as opposed to therapeutic, purposes should be submitted to the same routine as other donors, but obviously some decisions regarding their suitability to donate may be different (e.g. treatment with certain medications, or on the basis of medical history).

3. Individuals who attend a session and give the information that they are currently undergoing medical investigations or have been referred for a specialist opinion should be advised not to donate blood until investigations are complete, even if asymptomatic on the day.

4. Donors should be made aware that recipients are at risk from transfusion, and donors should therefore be asked to report any illness developing subsequent to the donation.

5. Information which is, or may be, of relevance to the health of the recipient and which arises subsequent to the transfusion of the blood, should be reported to the appropriate party e.g. hospital blood transfusion laboratory so that further action may be taken if deemed necessary.

6. The record of physical assessment and medical history of the donor must be identified by the examiner's signature. Any reason for exclusion should be recorded.

7. Donors following their normal meal pattern may be accepted. For donors presenting who have missed their normal meal, a cup of fluid and biscuits should be offered at the session prior to collection of the blood.

1.4 **Examples of conditions necessitating permanent exclusion**

This list is not exhaustive. Specific information may be obtained by referring to the current documents on Medical Assessment of Donors produced by the Blood Transfusion Service.

1.4.1 Cardiovascular diseases.
Individuals with circulatory disorders are especially subject to cardiovascular and cerebrovascular disturbances resulting from sudden haemodynamic changes. Thus all such donors are excluded.

1.4.2 Central nervous system diseases

In general, these conditions are contra-indications to donation, as the individual may well be unduly susceptible to sudden haemodynamic changes. In addition, those conditions known or suspected to be of viral origin, should be reason for exclusion.

1.4.3 Gastrointestinal diseases

All diseases which render the individual liable to iron deficiency through impaired iron absorption or blood loss should be reason for exclusion.

1.4.4 Hematological disease

Any disorder which may be of malignant potential (e.g. polycythaemia and other myeloproliferative disorders) should be reason for permanent exclusion.

1.4.5 Certain infectious diseases should result in permanent exclusion. These include:-

- AIDS, HIV infection
- Brucellosis
- Granuloma Inguinal
- Hepatitis C
- Kala Azar
- Lymphogranuloma venereum
- Q fever
- Syphilis
- Trypanosomiasis cruzi (Chagas disease)

1.4.6 Certain metabolic diseases should result in permanent exclusion.

1.4.7 Renal diseases

All chronic renal diseases are a reason for permanent exclusion.

1.4.8 Respiratory diseases.

Individuals who have significant chest disease should not be accepted as blood donors.

1.4.9 Creutzfeldt-Jakob disease

Individuals at risk of developing Creutzfeldt-Jakob disease must be permanently excluded.

1.4.10 Malignancy.
Diseases of malignant origin should be cause for permanent exclusion, although exceptions may be made for localized conditions at the conclusion of successful therapy.

1.5 Pregnancy

Pregnant and lactating women should not normally give blood in view of their high iron requirements at this time.

1.6 Donors on treatment with drugs

1.6.1 Donor deferral for most drugs is based on the underlying illness suffered by the donor rather than for the properties of the drug itself e.g. cardiovascular disease, diabetes, anemia and malignancies.

However, since in general traces of drugs in blood and blood components are believed to be harmless to patients, many people taking medications, when prescribed are acceptable as blood donors as long as the reason for which the medication is taken as acceptable.

A pragmatic view should be taken of treatment of infections with antibiotics. Providing the donor is in good health deferral is limited to one week after cessation of antibiotic therapy. This is based on what may be regarded as a reasonable recovery period for the infection and is not related to the antibiotic therapy itself.

1.6.2 Donors taking drugs which are proven or potentially teratogenic (e.g. vitamin A derivatives) or who are taking drugs which accumulate in tissues over long periods, should not be accepted for blood donation. The period of deferment after finishing a course of treatment should be determined individually for each drug in these categories.

1.6.3 Sporadic self-medication with some drugs (e.g vitamins, aspirin, sleeping tablets) need not prevent a donation being accepted, providing the donor is fit and well.

1.6.4 If the donor has taken drugs affecting platelet function (e.g. aspirin) within the last 5 days, the donations should not be used for the preparation of platelets. A list of all such drugs should be made available to staff at blood collection sessions by the Incharge of Blood Transfusion Centre.

1.6.5 Other drugs or tablets may be acceptable. The taking of some drugs may indicate a disease which would automatically make a donor ineligible.

1.6.6 Donors taking part in a clinical trail of drug therapy should be deferred until the trial is completed. Acceptability would then depend on the type of drug and its dosage, if the donor continues to take it prophylactically.
1.7 Infectious diseases

1.7.1 HIV and other blood borne infections including hepatitis B and hepatitis C

1. All potential donors must be provided with information so that those at risk will refrain from donation.

2. There is no evidence to suggest that hospital staff involved in caring for patients infected with these viruses or working in hospital laboratories, are at any greater risk with respect to infection than the general public. Such persons may be accepted as donors, providing that they have not suffered an inoculation injury or suffered contamination of non-intact skin with blood from an individual infected with HIV, HBV or HCV.

1.7.2 Hepatitis

Individuals with a history of jaundice or hepatitis should only be considered as blood donors 12 months after recovery from the illness. At the time of donation, approved tests for HBsAg and anti-HCV should be negative.

1. Risk groups

All persons who have received a transfusion of blood or blood products, acupuncture (other than as specified in the current documents on Medical Assessment of Donors produced by the Blood Transfusion Service), tattooing and ear-piercing should be deferred for 12 months.

2. Circumstantial involvement

Donors without demonstrable markers of hepatitis who have donated blood to two patients strongly suspected of having transfusion-transmitted hepatitis should be permanently excluded. The only donor of blood to a recipient who developed transfusion transmitted hepatitis, should also be excluded.

3. Return of Donors with Acute HBV Infection to Active Panel

Blood donors found to have had an acute hepatitis B infection with or without symptoms of disease can be considered eligible for re-admittance to the active donor panel provided one year has elapsed since the acute episode, there was clearance of HBsAg within six months and that a level of > 0.1 IU/ml of anti-HBs can be demonstrated in their serum.

This recommendation applies only to donors who have previously been negative for HBsAg and does not apply to known carriers of HBsAg who have lost HBsAg over protracted periods of time. Neither does it apply to donors found to have anti-HBc as a solitary marker in their serum. The reasonable expectation of an absence of integrated hepatic HBV DNA (and hence termination of infection) following recovery is only tenable for those individuals demonstrated to have undergone an acute self-limiting infection.
1.7.3 Reinstatement of donors whose serum has been confirmed to be falsely reactive in a microbiology assay, See Annex 3.2.2.6

1.8 Tropical diseases

1.8.1 Trypanosomiasis (Cruzi)

This may lead to an acute or chronic, incurable and even fatal illness. Blood from donors who have visited or lived in rural South America or Central America including Southern Mexico should ONLY be used for preparing plasma fractions (not plasma for clinical use or cryoprecipitate).

Donations from such persons may be used for normal purposes provided they have been shown by suitable tests to be free of antibodies to Trypanosoma Cruzi.

1.8.2 Filariasis, Kala Azar, Q Fever and Yaws

These are contra-indications to blood donations even after recovery has occurred

1.8.3 Amoebic dysentery, Schistosomiasis and Arthropod-borne encephalitides

These are not contra-indications to donation once recovery has taken place. A period of 2 years should be allowed after recovery from relapsing fever.

1.8.4 Malaria, exclusion for six months after diagnosis and treatment

1.9 Inoculations and immunizations

1.9.1 Prospective donors who have been immunized recently and are symptom-free may be accepted after the following:-

- Live attenuated vaccines: 3 weeks
- Killed vaccines: 48 hours
- Recombinant vaccine: 48 hours

Note:- Rabies vaccine

(a) 48 hour deferral if non-exposed
(b) for immunization after history of animal bite, defer until fully cleared by treating physician and 1 year following exposure.

Donors who have recently been actively immunized may have suitable levels of immune antibodies to merit donation for specific immune plasma.

1.9.2 Immunoglobulins administered after a known exposure can prolong the incubation period of a disease, hence the deferral period should be as follows.

- Anti-tetanus 1g: 4 weeks
- Normal human 1g: 6 weeks
- Hepatitis B 1g: 1 year
1.9.3 Normal human immunoglobulin administered prophylactically prior to going abroad does not in itself merit deferral although the country visited may do so.

1.10 Physical examination of donors

1.10.1 General considerations

Most donors may be accepted on the basis of medical history, general appearance and hemoglobin estimation, although it is advisable to examine the pulse and check the blood pressure.

This procedure, used skillfully, will lead to rejection or deferment of most donors who are unfit to be bled and it should be carried out meticulously. When in doubt, it is better to reject or defer and the Medical Officer or relevant authorized staff should ensure that an appropriate entry is made on the donor's record.

1.10.2 Inspection of donor

The donor should appear to be in good health. Note should be taken of poor physique, debilitation, undernutrition, plethora, jaundice, cyanosis, dysponea and mental instability. Suggestion of intoxication either by alcohol or narcotic drugs should be a reason to exclude that donor. The skin at the venepuncture site should be free from lesions.

1.10.3 Weight

Healthy individuals can generally donate up to 500 ml of blood (plus small laboratory sample) without any deleterious effect on their health. A standard blood donation is 450 ml ± 10% with optimum blood/anticoagulant ratio of 7:1 (See Annex 1). Those who weigh less than 50 kg (12 lbs) are more likely to suffer adverse effects (in particular dizziness and fainting) after a standard blood donation as this represents a greater proportion of their blood volume. Potential donors who weigh less than 50 kg may give a smaller donation with the anticoagulant content adjusted accordingly, but all such donors should be assessed carefully to ensure that the low body weight is not due to illness.

1.10.4 Haemoglobin Estimation

Hemoglobin concentration should be determined each time a potential donor presents. The acceptable lower limits are female donors 12.5 g/dl, or male donors 13.5 g/dl. The type of test is left to the discretion of the consultant at the Transfusion Centre in charge of the selection and care of donors.

Potential donors whose hemoglobin appears to be below the appropriate concentration should not be bled. It is recommended that a check of the concentration is made using an alternative method. The reason for deferral should be explained to such donors and they should be advised to see their own GP if this is considered to be appropriate.
Where a quantitative method of Hb estimation is employed and acceptable upper limit for donation should be set at the normal upper limit for the method used. Individuals with significantly high Hb levels should be investigated and referred appropriately.
Chapter 2
Quality Assurance at Blood Donor Sessions

2.1 General Specifications

2.1.1 General Comments

1. This section applies to the collection of donations of whole blood at permanent sites or by mobile blood collections teams.

2. The ultimate responsibility for the correct safe procedure for the collection of blood is that of the Medical Director or equivalent; the immediate responsibility for the operation of the blood collection session is that of the medical practitioner or senior nurse in attendance.

3. Each Transfusion Centre must prepare its own procedures manual, covering all phases of activity of blood collection. Numbered copies of the procedures manual should be issued to all staff involved in sessions procedures and measures should be instituted to ensure that every copy is regularly updated.

4. The staff should be trained for venepuncture.

2.1.2 Guidance for the following procedures is given in Annex 1:

DONOR IDENTIFICATION

HAEMOGLOBIN OR HAEMATOCRIT SCREENING
Copper sulphate hemoglobin screen
Copper sulphate storage
Copper sulphate for routine use
Copper sulphate procedure: finger prick blood sample
Spectrophotometric method for haemoglobin screening
The microhaematocrit method for haemoglobin screening

PREPARATION OF THE VENEPUNCTURE SITE

PREPARATION OF THE BLOOD PACK PERFORMANCE

OF THE VENEPUNCTURE

BLOOD DONATION
Blood anti coagulation
Blood flow
Blood volume monitoring by spring balance
Sample collection
Completion of the donation
Final inspection
Safety related defects
2.1.3 Guidance for laboratory testing procedures is given in Annex 3.

2.2 Records

2.2.1 Donor identification

1. The identity of the donor must be recorded and linked to the donation records.

2.2.2 Donation identification

1. Sessional reception staff must ensure that a unique number set is assigned to each donation. Great caution is necessary to avoid crossover or duplication of numbers.

2. Sets of numbers not used should be placed in container for destruction and must be accounted for.

3. If there is need to renumber a blood pack system, new numbers should be used; labels which have been discarded shall not be retrieved.

2.2.3 Labelling

1. Donor session staff must ensure that the unique number assigned to the donation appears on the donor session record, the primary and secondary collection packs and all the sample tubes used.

2. The organization should be such as to avoid the possibility of errors in the labelling of blood containers and blood samples; for example, the taking of samples at the end of a donation should be directly linked with the cessation of the donation with the minimum possible time interval and the blood bag and the corresponding samples should not be removed from the donor's couch until a satisfactory check on correct labelling has been carried out.

For this purpose, it is recommended that each donor couch has its own individual facilities for the handling of samples during donation and labelling.

2.2.4 Donor Session Records

1. A record of the sessions venue, the date, the donation number and the identity of all donors attending must be maintained.

   For any donors who are deferred, rejected or retired, the full details must be recorded and the reasons given for the action taken.

2. The records of blood donation session should allow identification of each important step associated with the donation.

   All successful donations must be recorded; unsuccessful donations must be recorded together with the reason why they were unsuccessful, all adverse reactions must be
recorded together with the action taken; full details of any other incidents, including those involving only staff must be recorded.

3. These records should be used for the regular compilation of statistics which should be studied minutely by those responsible for activities concerned with the organization and management of blood collection sessions.

2.3 Documentation

2.3.1 Selection of donors see Chapter 1 of Section 1.

2.3.2 Specification of blood and blood products see Chapter 3 and 4

2.4 Control of Purchased Material and Services

2.4.1 Specification and inspection of blood bags

1. Blood collection shall be by aseptic techniques using a sterile closed system and a single venepuncture. The integrity of the system must be checked prior to use and measures must be taken to prevent unsterile air entering the system.

2. Blood shall be collected into containers that are pyrogen free and sterile, containing sufficient licensed anticoagulant for the quantity of blood to be collected.

3. The container label shall state the kind and amount of anticoagulant, the amount of blood that can be collected and the required storage temperature.

4. Manufacturer's directions regarding storage, use and expire dates of the packs whose outer containers have been opened and resealed must be adhered to.

5. Batch number of the blood packs used should be recorded.

6. The donation number on the packs and sample tubes should be checked at the end of the donation to ensure that those for a given donation are identical.

7. Prior to release from the blood collection session the pack and its associated tubing should be reinspected for defects and its integrity should be checked by applying pressure to the pack to detect any leaks. Any defective pack should be marked for disposal and held separately from intact packs. Details of the defect (s) should be recorded for future analysis and action (see Annex 1,6.8 and 6.9)

2.5 Collection Control

Guidance on the selection of premises for donation sessions is given in Annex 2.

2.6 Protection and Preservation of Product Quality

Guidance on requirements for labelling, storage and transportation is given in Chapter 3.
Chapter 3

General Guidelines for Blood Component Manufacture

3.1 Scope of the Guidelines

3.1.1 These guidelines provide a framework on which BTCs should assemble standard operating procedures for the manufacture of blood components.

3.1.2 These guidelines apply to single donor and small pool components (<12 donors) prepared from units of whole blood or by apheresis.

3.1.3 BTCs should ensure hospital laboratories in their Region are informed of these Guidelines.

3.2 Setting and Maintenance of Specifications

3.2.1 The wide variability of the source material from which blood components are prepared makes it difficult to set stringent limits. Nevertheless, realistic minimum specifications should be set and complied with.

3.2.2 Component and process quality monitoring results should be subjected to statistical analysis so that trends can be identified.

3.2.3 If the results of analysis show a consistent trend away from the minimum requirements the cause should be investigated. The criteria to be investigated will be detailed in the relevant Standard Operating Procedure (SOP) together with the corrective action to be taken although the steps to be considered should include the following:

1. An investigation of the testing and production procedures.
2. Checking that SOPs are up to date and followed.
3. Checking the operation of equipment and storage conditions.
4. The person responsible for quality assurance and/or production may initiate investigations beyond the scope of written procedures.

3.3 Component and Process Monitoring Tests

3.3.1 Certain tests are performed on every component unit. Red cell serology and certain microbiological screening tests are mandatory quality control procedures since the test results have a direct bearing on the release of the final component.

3.3.2 These guidelines also indicate the minimum level of additional testing necessary to ensure components are prepared to specification.

3.3.3 Each component should be visually inspected at each stage of processing and immediately prior to issue. The component must be withdrawn if there is evidence of leakage, damage to or fault in the container, excessive air, suspicion of microbial contamination.
contamination or any other centra-indications such as unusual turbidity, haemolysis or other colour change.

3.3.4 Sampling Procedures

1. Sampling procedures should be designed and validated to ensure the sample truly reflects the contents of the component pack.
2. Where test samples are removed from a component to be issued for transfusion, the sampling procedure should be designed and validated to ensure the sterility and essential properties of the component are not adversely affected.

3.3.5 Frequency of Tests

The regularity with which components are made influences the frequency with which component and process monitoring tests are required.

1. The target minimum testing frequency is 1% of the annual production of each component or 10 of each component type per month, whichever is greater.

2. If a component is made, on average, less than 10 times per month the additional tests described in the specifications should be performed on every component unit.

3. For leucocyte depleted components, the manufacturer should additionally ensure that all components are within specification for leucocyte count before release to stock (eg by a recognised process control methodology or by performing leucocyte counts on 100% of leucocyte depleted components).

4. The testing protocol should take into account all variables and ensure samples are taken across these variables.

3.3.6 Component Weight: Volume

1. To provide information, which is useful for clinicians, the component specifications given in Chapter 6 generally require the component label to indicate a volume. This may be either the calculated volume or nominal volume and the nominal volume may be based on a national or locally established volume specification.

2. Since volume generally is calculated by dividing the component weight by its specific gravity, to ensure some element of standardisation the following conventions should apply:

(i) Whole blood volume is most appropriately calculated by deducting the weight of the pack assembly and anticoagulant and dividing the resulting weight by the nominal specific gravity of 1.06.

However, when whole blood is issued as a component, the volume given on the component label should include whole blood and anticoagulant.
(ii) For red cell components, volume is calculated by weighing the pack, deducting the weight of the pack assembly only and dividing the resultant weight by the nominal specific gravity 1.06. The weight of anticoagulant and, if relevant, additive solution are not deducted when calculating the volume of red cell components.

(iii) For platelets and plasma components, volume is calculated by weighing the pack, deducting the weight of the pack assembly and dividing the resulting weight by the nominal specific gravity of 1.03

3.3.7 Requirement to Meet Specifications

For mandatory microbiology screening tests, all components must meet specification. Leucocyte depleted components must meet the specified leucocyte count.

With the exception of these tests, because of biological variability, it is acceptable if a minimum of 75% of the results of component and process monitoring tests achieve the specification.

3.4 Component Processing

3.4.1 The Starting Material

The starting material for component preparation is whole blood or the products of apheresis collected from donors who satisfy current donor selection criteria. Components must be collected into blood packs/apheresis kits (including anticoagulant/additive solutions) that are licensed by the Drug Control Authority.

Starting material for component preparation should be transported as described in 3.10.2.

3.4.2 Separation of components for Direct Clinical Use

The timing and method of separation depends on the components to be prepared from a given donation. Platelets and plasma components should be separated and placed under validated, controlled storage, conditions normally within 8 hours of venepuncture.

3.4.3 Prevention of Microbial Contamination

1. Infection associated with the microbial contamination of blood and blood components still occurs. Whilst there is no evidence to suggest that routine sterility testing of blood components diminishes or eliminates such instances of infection, the following measures will minimise the risks:

(i) Creating and maintaining the highest level of awareness among all personnel of the constant care and attention to detail needed to minimise microbial contamination e.g. validation and periodic monitoring of the effectiveness of venepuncture site preparation.
(ii) The use of validated procedures designed to minimise microbial contamination of the environment and prevent microbial contamination of components.

(iii) Monitoring of the microbial load in equipment and in the environment of component preparation areas.

2. It is important that data derived from such monitoring exercises are accumulated and regularly examined with a view to taking appropriate action.

3. Closed System

(i) The term “closed system” refers to a system in which the blood pack assembly is manufactured under clean conditions, sealed to the external environment and sterilized by an approved method. Apart from the act of blood collection, when a needle is exposed and enters the donor’s arm, the integrity of this assembly must not be breached in any way.

(ii) When a Sterile Connection Device is used the system can be regarded as closed providing that the process of joining and sealing has been validate and shown not to lead to the possibility of microbial contamination of the component. Seal efficiency should be inspected to a standard protocol.

(iii) A closed system is also provided by the use of a validated procedure that incorporates and approved microbial filter.

(iv) There is no need to undertake sterility testing of components prepared in a closed system.

4. Open System

(i) The term “open system” refers to a system in which a breach has occurred but where every effort is made to prevent microbial contamination by operating in a clean environment, using sterilized materials and aseptic handling techniques.

In such circumstances, positive pressure should be exerted on the original containers and maintained until the container is sealed. Open system processing should be undertaken in a designated clean environment.

The sterility of components prepared in an open system should be monitored using validated methods.

(ii) Blood components prepared by an open system should be used as soon as possible. If storage is unavoidable, components with a recommended storage temperature of 22°C ± 2°C should be used within 6 hours. Components with a recommended storage temperature of 4°C ± 2°C should be used within 24 hours.

5. Components are rendered unsuitable for clinical use when breached and the requirements defined for an open system have not been observed.
6. Any new development in component preparation by an open procedure must be validated to ensure the maintenance of sterility before the procedure can be used to produce components for therapeutic use.

7. Procedures for collecting samples for sterility testing must not adversely affect the sterility of components intended for subsequent transfusion.

3.5 Component Shelf Life

To provide an unequivocal definition of component dating periods the following conventions should apply:

3.5.1 Where components are pooled, the maximum shelf life of the pool must not exceed the expiry date of the oldest constituent component.

3.5.2 Blood components prepared by an open system should be used as soon as possible. If storage is unavoidable, components with a recommended storage temperature of 22°C ± 2°C should be used within 6 hours. Components with a recommended storage temperature of 4°C ± 2°C should be used within 24 hours.

3.5.3 For all other components the date of collection will be assigned day 0 of the shelf life. Day 1 of storage will commence at 1 minute past midnight on the day after collection.

3.6 Component Labelling

3.6.1 Bar-coded labels and associated technology must be used whenever possible.

3.6.2 The design and use of labels should conform with specifications set out by the relevant Blood Transfusion Services/Authorities. See Annex-5.

3.6.3 Procedures should be established to ensure labels are satisfactory for their intended use.

3.6.4 Labels to be attached to blood components should be stored under secure conditions and used with care.

3.6.5 Donation/Donor Identification

1. The use of a unique bar coded/eye readable donation number links the donation to its donor. Donation numbers must be attached to all integral packs, sample tubes and corresponding record documents at the time of donation.

2. When component production requires the use of subsidiary packs which are not an integral part of the pack assembly e.g. filtration, freezing, a secure system must be in place to ensure that the correct eye readable or bar-coded donation number is placed on each additional pack used.

3. To ensure that all constituents of a component pool can be traced, a unique batch number must be assigned to the pool and placed on the pack containing the pool. Alternatively, the unique donation number of each constituent component should appear on the pack containing the component pool.
4. When a component is divided a secure system must be in place to ensure that all sub batches can be traced.

3.7 Component Storage

3.7.1 Specifications for Component Storage Areas

1. Storage areas for blood components must operate within a specified temperature range and should provide adequate space suitable lighting and be arranged and equipped to allow dry, clean and orderly storage.

2. Good Manufacturing Practice requires that components of different status are appropriately identified and effectively separated.

   Recognised status categories include;

   (i) Quarantine

   Procedures should ensure that untested components are not quarantined with components which have produced, or are likely to produce repeatedly reactive results in mandatory microbiological screening tests.

   Secure and exclusive quarantine storage should be available for known biohazard material awaiting disposal (see 3.8.2).

   (ii) Non-Conforming

   Components which do not comply with the specification for mandatory test or are otherwise unsuitable for transfusion should be categorised as non-conforming and disposed off accordingly,

   (iii) Returned

   Components which are returned from blood transfusion laboratories outside the direct control of the BTC normally should not be returned to stock. Components which are returned to the BTC but which have been maintained within specification should be held securely pending possible re-instatement to stock by a designated person.

   (iv) Stock

   Components which have been deemed satisfactory for issue by a designated person should be held in stock.

3. Appropriate security and status labelling of component storage areas is essential.

4. A current inventory should be maintained of components in each storage category.

5. Areas/equipment in which components are to be stored should be validated before their introduction into routine use and periodically thereafter.
A permanent, continuous record of storage temperature should be made and stored.

3.7.2 Procedures for Component Storage

Written procedures must be established for the storage of blood components. These include the following:

1. A procedure to ensure components are not released to stock unless authorised by a designated person.

2. Definitions of the designated storage areas including the storage specification, the status of components to be stored in each area and the persons who are authorised to access each area.

3. Procedures for validating and monitoring the conditions of storage.

4. Procedures for ensuring the good order and cleanliness of storage areas.

5. Procedures to ensure the storage of blood components does not jeopardise their identity, integrity or quality.

6. A procedure which ensures appropriate stock rotation.

3.8 Discard of Non-Conforming Components

3.8.1 Procedures for the discard of non-conforming components should ensure that an appropriate record of discard is maintained. This includes:

* the donation number
* the component identity
* the reason for discard
* the date of discard
* the identity of the person effecting the discard

3.8.2 Biohazards

1. Components from donations that are repeatably reactive in mandatory microbiological screening tests or from donors whose records indicate their components should be destroyed because of previous mandatory test results are classified as biohazards.

2. Secure and effective procedures are required to ensure that all components and samples from biohazard donations are retrieved and inactivated before their disposal. In addition to 3.8.1, this includes:

* a system which ensures all components prepared from any donation can be traced.
* maintaining a record of the person who retrieves each biohazard component, including laboratory samples,
* a procedure to ensure biohazard material has been inactivated before disposal.
3. When biohazard material, eg plasma, is retained for laboratory use, it must be appropriately labelled to prevent it ever being used for therapeutic purposes and must be stored in a secure freezer or other storage unit that is clearly labelled to prohibit the storage of material for therapeutic use. An inventory of freezer (or other storage unit) contents of such samples, record of "sample" retention, reason for retention, and ultimate fate should be maintained.

3.9 **Component Release**

3.9.1 All components must be appropriately labelled in accordance with these guideline specifications including those general guidelines outlined in 3.6.

3.9.2 Standard procedures must ensure that blood and blood components cannot be released to stock until all the required laboratory tests, mandatory and additional, have been completed, documented and approved within a validated system of work and it has been ascertained that conditions of production and storage have been satisfactory. Compliance with this requirements may be achieved by:

1. The use of a computer programme, or suite of programmes, which requires the input of valid and acceptable test results for all the mandatory and required laboratory tests before permitting, or withholding, the release of each individual unit.

2. Where a computer-based system is not used, documented approval for the release of each individual unit by a designated person.

3. Where the computer-based system is temporarily unavailable, it is necessary to revert to the procedure in 3.9.2.2.

3.10 **Transport of Blood components**

See also Annex 4

3.10.1 **General Considerations**

1. Blood components should be transported in containers which have been validated for the purpose.

2. Transport containers should be appropriately labelled and should be secure and protect components from damage during transit.

3. Documentation should accompany components in transit to permit their identification.

4. Transport containers should not be exposed to temperatures beyond the range for which they have been validated.

5. Where melting ice is used to achieve an appropriate storage temperature, it should not come into direct contact with the components.

6. Dead air space in packaging containers should be minimised.
7. Written procedures for the transportation of components should be established and should ensure that the guidance given in 3.11.1 to 3.11.1.6 is complied with. In addition, written procedures should include the following:

(i) Definition of approved systems of packaging, transportation and transport conditions required for each component (see Chapter 4).

(ii) A procedure for monitoring approved systems of packaging and transportation.

3.10.2 Transportation From Collection Site to Processing Centre

1. Blood from donor sessions must be transported under conditions validated to be suitable for the various components to be prepared from the donations.

2. Blood being transported from donor sessions must be accompanied by documentation, which ensures that all donations can be accounted for. (NB "documentation" includes information in writing or in electronic format).

3.10.3 Transport of Components from BTCs to Hospitals/Users

1. Blood components should be transported under conditions which are as close as possible to their specific storage requirements. (See Chapter 4). Transport time should be kept to a minimum.

2. Components despatched from a BTC should be accompanied by a despatch note detailing as a minimum the donation number of each component and, if relevant, their blood group. The despatch note should also contain the signature(s) and designation of the person(s) responsible for the issue and of the person receiving the consignment. A copy of the signed and annotated despatch note should be returned to the BTC for storage.

3.11 Component Recall

3.11.1 There must be a documented system available in each BTC whereby adverse effects caused by the administration of any component can enable the recall, if appropriate, of all unused components derived from that donation or all donations which are a constituent of a component pool.

3.11.2 Similarly, there must be a documented system in each BTC for the recall of any component or constituent of a component pool where reasonable grounds exist for believing it could cause adverse effects.

3.11.3 Any recall of a component should lead to a thorough investigation with a view to preventing a recurrence.
Chapter 4

Guideline Specifications for Blood Components

4.1 Whole Blood

4.1.1 General Description

A unit of blood collected into an anticoagulant and not further processed.

Whole blood from which certain cellular or plasma elements have been removed as an operational expedient rather than for a specific clinical indication can be labelled as whole blood provided it meets the specification given at 4.1.5.

4.1.2 Technical Information

A unit of whole blood consists of 450ml ± 45ml of blood from a suitable donor (see Chapter 1) in an approved container (see Chapter 3) containing anticoagulant (normally 63ml). Donations of 250ml or less could also be used, if suitable collection packs are available.

4.1.3 Labelling (for general guidelines see 3.6).

The following shall be included on the label.

- whole blood and total volume (ie including anticoagulant)
- the producer's name in eye readable and BTS approved barcode format
- the donation number
- the ABO group ;
  the RhD group stated as positive or negative
- the composition and volume of the anticoagulant solution
- the date of collection and expiry date
- the temperature of storage

In addition, the following statements should be made:

CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information.

4.1.4 Storage (for general guidelines see 3.7)

1. Whole blood may be stored for a maximum of 35 days at a core temperature of 4° C ± 2° C if an adenine supplemented anticoagulant is used, otherwise the maximum period of storage is 28 days at a core temperature of 4° C ± 2° C
2. Variation from the core temperature of 4°C ± 2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.

3. Exceptionally, i.e. due to equipment failure at a BTC, whole blood which has been exposed to a core temperature not exceeding 10°C and not less that 1°C may be released for transfusion provided:

   • that the component has been exposed to such a temperature change on one occasion only
   • that the duration of the temperature increase has not exceeded 5 hours
   • that a documented system is available in each BTC to cover such eventualities
   • that adequate records of the incident are compiled and retained

4.1.5 Testing

1. In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, a minimum of 75% of those components tested for the parameter shown at 4.1.5.2 below shall meet the specified value.

2. Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1%</td>
<td>513ml ± 45ml</td>
</tr>
</tbody>
</table>

4.1.6 Transportation (for general guidelines see 3.10)

The air temperature of transport containers for units of whole blood should be maintained between 2°C and 10°C during transportation from the BTC to the place that they are intended for use. Transport time under these conditions normally should not exceed 12 hours.

4.2 Red Cells in Additive Solution

4.2.1 General Description

A component prepared by removing most of the plasma from whole blood after centrifugation. The red cells are suspended in an additive solution.

4.2.2 Technical Information

The volume of remaining plasma will influence the hematocrit of this component.

4.2.3 Labelling (for general guidelines see 3.6)

The following shall be included on the label

- red cells in additive solution
- the producer's name in eye readable and BTS approved barcode format
- the donation number
- the ABO group
Standards and Guidelines for Stood Transfusion Services, Pakistan.

- the RhD group stated as positive or negative
- the composition and volume of the additive solution
  the date of collection and expiry date
- the temperature of storage

In addition, the following statements should be made

CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

4.2.4 Storage (for general guidelines see 3.7)

1. Red cells in additive solution may be stored for a maximum of 35 days at a core temperature of 4°C ± 2°C.

2. Variation from the core temperature of 4°C ± 2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.

3. Exceptionally, i.e. due to equipment failure at a BTC, red cells in additive solution which have been exposed to a core temperature not exceeding 10°C and not less than 1°C may be released for transfusion provided:
   - that the component has been exposed to such a temperature change on one occasion only
   - that the duration of the temperature change has not exceeded 5 hours
   - that a documented system is available in each BTC to cover such eventualities
   - that adequate records of the incident are compiled and retained

4.2.5 Testing

1. In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, a minimum of 75% of those components tested for the parameters shown at 4.2.5.2 below shall meet the specified values.

2. Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1%</td>
<td>350ml ± 70ml</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>1%</td>
<td>0.50 to 0.70</td>
</tr>
</tbody>
</table>

4.2.6 Transportation (for general guidelines see 3.10)
The air temperature of transport containers for units of red cells in additive solution should be maintained between 2°C and 10°C during transportation from the BTC to
the place that they are intended for use. Transport time under these conditions normally should not exceed 12 hours.

4.3 Red Cells, Leucocyte Depleted

4.3.1 General Description
A red cell component containing less than 5 x 10⁶ leucocytes.

4.3.2 Technical Information
1. Leucocyte depletion can be achieved by a number of methods which should be validated before use.

2. If filtration is used the recommended capacity of the filter should not be exceeded.

3. Leucocyte depletion procedures should not reduce red cell volume by more than 15%.

4. If the leucodepletion process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct donation number is put on the final component pack.

4.3.3 Labelling (for general guidelines see 3.6)
The following shall be included on the label
- red cells leucocyte depleted and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number
- the ABO group
- the RhD group stated as positive or negative
- the composition and volume of the anticoagulant solution
- the date of collection and expiry date and time
- the temperature of storage

In addition the following statements should be made

CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

4.3.4 Storage (for general guidelines see 3.7)
1. If prepared in a closed system, red cells, leucocyte depleted may be stored for a maximum of 35 days at a core temperature of 4°C ± 2°C if an adenine supplemented anticoagulant is used, otherwise the maximum period of storage is 28 days at a core temperature of 4°C ± 2°C.
2. Red cells, leucocyte depleted prepared by an open procedure should be used as soon as possible. If storage is unavoidable, the component should be stored at a core temperature of 4°C ± 2°C and used within 24 hours.

3. Variation from the core temperature of 4°C ± 2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.

4. Exceptionally, i.e. due to equipment failure at a BTC, red cells, leucocyte depleted which have been prepared in a closed system and exposed to a core temperature not exceeding 10°C and not less than 1°C may be released for transfusion provided:
   - that the component has been exposed to such a temperature change on one occasion only
   - that the duration of the temperature change has not exceeded 5 hours
   - that a documented system is available in each BTC to cover such eventualities
   - that adequate records of the incident are compiled and retained

4.3.5 Testing

1. In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, the manufacturer must ensure (e.g. by a recognised process control methodology or by performing leucocyte counts on all components) that leucocyte depleted components meet their specification before they are released to stock as "leucocyte depleted". Furthermore, a minimum of 75% of those components tested for the other parameters shown at 4.3.5.2 below shall meet the specified values.

2. Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1%</td>
<td>locally specified volume range</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>1%</td>
<td>0.55 to 0.75</td>
</tr>
<tr>
<td>Leucocyte Count*</td>
<td>As per 4.3.5.1</td>
<td>&lt;5x10⁶/unit</td>
</tr>
</tbody>
</table>

*Methods validated for counting low levels of leucocytes must be used

4.3.6 Transportation (for general guidelines see 3.10)

The air temperature of transport containers for units of red cells, leucocyte depleted should be maintained between 2°C and 10°C during transportation from the BTC to the place that they are intended for use. Transport time under these conditions normally should not exceed 12 hours and if open processing has been used should be as short as possible.

**Red Cells (Washed)**

4.4.1 General Description
A red cell component from which most of the plasma, leucocytes and platelets have been removed by washing with 0.9 % w/v sodium chloride for injection.

4.4.2 Technical Information

1. The amount of residual protein will depend on the washing protocol. Washing can be performed by interrupted or continuous flow centrifugation.

2. The use of validated washing procedures that incorporate chilled saline, at least for the final wash, is recommended. This will minimise the risk of bacterial contamination and helps to produce a component that meets the transit temperature requirements (see 4.4.6).

3. A secure system must be in place to ensure the correct donation identification number is put on the component pack of red cells, washed.

4.4.3 Labelling (for general guidelines see 3.6)

The following shall be included on the label:
- red cells, washed and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number
- the ABO group
- the RhD group stated as positive or negative
- the composition and volume of the suspending solution
- the date and time of preparation and expiry date and time
- the temperature of storage

In addition, the following statements should be made:
CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

4.4.4 Storage (for general guidelines see 3.7)

Red cells, washed should be used as soon as possible. If storage is unavoidable, or if an open system of preparation has been used, the component should be stored at a core temperature of 4°C + 2°C and used within 24 hours.

4.4.5 Testing

1. In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, a minimum of 75% of those units components tested for the parameters shown at 4.4.5.2 below shall meet all the specified values.
2. Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>10 per month or, if made less frequently, every component</td>
<td>280ml ± 60ml</td>
</tr>
<tr>
<td>Haematocrit</td>
<td></td>
<td>0.65 to 0.75</td>
</tr>
<tr>
<td>Residual Protein</td>
<td></td>
<td>&lt;0.5g/unit</td>
</tr>
</tbody>
</table>

4.4.6 Transportation (for general guidelines see 3.10)
The air temperature of transport containers for units of red cells, washed should be maintained between 2°C and 10°C during transportation from the BTC to the place that they are intended for use. Transport times under these conditions normally should not exceed 12 hours and if open processing has been used should be as short as possible.
4.5 Platelets

4.5.1 General Description
A component prepared from whole blood normally within 8 hours of venepuncture, which contains platelets as the major cellular product.

4.5.2 Technical Information
1. The component must be prepared at ambient temperature before the red cell component is cooled to its storage temperature.
2. The volume of suspending medium must be sufficient to maintain the pH of the component throughout its shelf life.

4.5.3 Labelling (for general guidelines see 3.6)
The following shall be included on the label
- platelets and nominal volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number
- the ABO group
- the RhD group stated as positive or negative
- the date of collection and expiry date
- the temperature of storage and a comment that continuous gentle agitation throughout storage is recommended

In addition, the following statements should be made:

CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

NOTE: If pooled, the donation number of all contributing platelet components, or a unique batch or pool number must appear on the component label.

4.5.4 Storage (for general guidelines see 3.7)
1. The storage period depends on a number of factors including the nature of the container, the concentration of platelets and on whether an open or closed system is used.
2. Packs currently in use for this purpose allow for storage at a core temperature of 22°C ± 2°C for up to 5 days in a closed system. Gentle agitation must be maintained throughout the storage period.
3. After any open system manipulation, platelets should be used as soon as possible. If storage is unavoidable the component should be stored at a core temperature of 22°C ± 2°C with continuous gentle agitation and used within 6 hours.
4.5.5 Testing

1. In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, a minimum of 75% of those components tested for the parameters shown at 4.5.5.2 below shall meet the specified values.

2. Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1%</td>
<td>Within locally defined nominal volume range</td>
</tr>
<tr>
<td>Platelet count</td>
<td>1%</td>
<td>≥55x10⁹/unit</td>
</tr>
<tr>
<td>Leucocyte count</td>
<td>1%</td>
<td>&lt; 0.2x10⁹/unit</td>
</tr>
<tr>
<td>Ph at end of shelf life</td>
<td>1%</td>
<td>6.4-7.4</td>
</tr>
</tbody>
</table>

NOTE: Visual inspection of platelet components for the swirling phenomenon, clumping, excessive red cell contamination and abnormal volume is a useful pre-issue check.

4.5.6 Transportation (for general guidelines see 3.10)

Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22°C ± 2°C with continuous gentle agitation.

4.6 Platelets, Pooled (Leucocyte Depleted)

4.6.1 General Description

A pool of platelets which contains less than 5 x 10⁶ leucocytes.

4.6.2 Technical Information:

1. If filtration is used the recommended capacity of the filter should not be exceeded.

2. The volume of suspending medium must be sufficient to maintain the pH of the component throughout its shelf life.

3. If the leucodepletion process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct identification number is put on the final component pack.

4.6.3 Labelling (for general guidelines see 3.6)

The following shall be included on the label
- Platelets, pooled, leucocyte depleted and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number of all contributing platelet units or a unique batch or pool number
- the ABO group
- the RhD group stated as positive or negative
- the expiry date
- the temperature of storage and a comment that continuous gentle agitation throughout storage is recommended

In addition, the following statements should be made:

CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

4.6.4 Storage (for general guidelines see 3.7)

1. The storage period depends on a number of factors including the nature of the container, the concentration of platelets and on whether an open or closed system is used.

2. Pack currently in use for this purpose allow for storage at a core temperature of 22°C ± 2°C for up to 5 days in a closed system.

3. If any production stage involves an open system, after preparation the component should be used as soon as possible. If storage is unavoidable, the component should be stored at a core temperature of 22°C ± 2°C with continuous agitation and used within 6 hours

4.6.5 Testing

1. In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, the manufacturer must ensure (e.g. by a recognised process control methodology or by performing leucocyte counts on all components) that leucocyte depleted components meet their specification before they are released to stock as "leucocyte depleted". Furthermore, a minimum of 75% of those components tested for the other parameters shown at 4.6.5.2 below shall meet the specified values.

2. Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1% or 10 per month whichever is greater If less than 10 per month every component</td>
<td>Within locally defined nominal volume range</td>
</tr>
<tr>
<td>Platelet count</td>
<td></td>
<td>≥240x10⁹/pool</td>
</tr>
<tr>
<td>Ph at end of shelf life</td>
<td></td>
<td>6.4 - 7.4</td>
</tr>
<tr>
<td>Leucocyte count*</td>
<td>As per 4.6.5.1</td>
<td>&lt;5x10⁶/pool*</td>
</tr>
</tbody>
</table>

* methods validated for counting low levels of leucocytes must be used
NOTE: Visual inspection of platelet components for the swirling phenomenon, clumping, excessive red cell contamination and abnormal volume is a useful pre-issue check.

4.6.6 Transportation (for general guidelines see 3.10)

Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of \(22^\circ C \pm 2^\circ C\) with continuous gentle agitation.

4.7 Platelets, Apheresis

4.7.1 General Description
A component prepared from anticoagulated blood which is separated into components by a suitable apheresis machine with retention of the platelets and a portion of the plasma. The remaining elements may be returned to the donor. The donor screening procedure should be completed before the commencement of Apheresis.

4.7.2 Technical Information
1. Platelets may be collected by a variety of apheresis systems using different protocols. Since platelet yields may vary, each procedural protocol must be fully validated, documented and specifications set accordingly.
2. The volume of suspending medium must be sufficient to maintain the pH of the component throughout its shelf life.

4.7.3 Labelling (for general guidelines see 3.6)

The following shall be included on the label:
- Platelets, apheresis and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number
- the ABO group
- the RhD group stated as positive or negative
- the date of collection and expiry date
- the temperature of storage and a comment that continuous gentle agitation throughout storage is recommended

In addition, the following statements should be made:

CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information.

4.7.4 Storage (for general guidelines see 3.7)
1. The storage period depends on a number of factors including the nature of the container, the concentration of platelets and on whether an open or closed system is used.

2. Pack currently in use for this purpose allow for storage at a core temperature of 22°C ± 2°C for up to 5 days in a closed system.

3. The platelets obtained through apheresis should preferably be used on the same day.

4.7.5 Testing

1. In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, a minimum of 75% of those components tested for the parameters shown at 4.7.5.2 below shall meet the specified values.

2. Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1% or 10 per month whichever is greater If less than 10 per month, every component</td>
<td>Within locally defined nominal volume range</td>
</tr>
<tr>
<td>Platelet count</td>
<td></td>
<td>≥240x10⁹/ unit</td>
</tr>
<tr>
<td>Leukocyte count</td>
<td></td>
<td>&lt;0.8x 10⁹/unit</td>
</tr>
<tr>
<td>pH at end of shelf life</td>
<td></td>
<td>6.4 - 7.4</td>
</tr>
</tbody>
</table>
4.7.6 Transportation (for general guidelines see 3.10)

Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22°C ±2°C with continuous gentle agitation.

4.8 Platelets, Apheresis (Leucocyte Depleted)

4.8.1 General Description

A platelet component containing less than 5 x 10⁶ leucocytes

4.8.2 Technical Information

1. Platelets, apheresis, leucocyte depleted may be collected by a variety of apheresis systems using different protocols. Since platelet yields may vary, each procedural protocol must be fully validated, documented and specifications, set accordingly.

2. If filtration is used the recommended capacity of the filter should not be exceeded.

3. The volume of suspending medium must be sufficient to maintain the pH of the component throughout its the shelf life.

4. If the leucodepletion process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct identification number is put on the final component pack.

4.8.3 Labelling (for general guidelines see 3.6)

The following shall be included on the label

- Platelets, apheresis, leucocyte depleted and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number
- the ABO group
- the RhD group stated as positive or negative
- the date and time of preparation and expiry date and time
- the temperature of storage and a comment that continuous gentle agitation throughout storage is recommended

In addition, the following statements should be made:
CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

4.8.4 Storage (for general guidelines see 3.7)

1. The storage period depends on a number of factors including the nature of the container, the concentration of platelets and on whether an open or closed system is used.

2. Pack currently in use for this purpose allow for storage at a core temperature of 22°C ± 2°C for up to 5 days in a closed system.

3. Where any manufacturing step involves an open system the platelets should be used as soon as possible after collection. If storage is unavoidable, the component should be stored at a core temperature of 22°C ± 2°C with continuous agitation and used within 6 hours.

4. If the leuco depletion process transfers the final component.

4.8.5 Testing

1. In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, the manufacturer must ensure (e.g. by a recognised process control methodology or by performing leucocyte counts on all components) that leucocyte depleted components meet their specification before they are released to stock as "leucocyte depleted". Furthermore, a minimum of 75% of those components tested for the other parameters shown at 4.8.5.2 below shall meet the specified values.

2. Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1% or 10 per month whichever is greater</td>
<td>Within locally defined nominal volume</td>
</tr>
<tr>
<td></td>
<td>If less than 10</td>
<td>range</td>
</tr>
<tr>
<td>Platelet count</td>
<td>Per month, every component</td>
<td>≥ 240 x 10⁹/unit</td>
</tr>
<tr>
<td>PH at end of shelf life</td>
<td></td>
<td>6.4 - 7.4</td>
</tr>
<tr>
<td>Leucocyte count*</td>
<td>As per 4.8.5.1</td>
<td>&lt; 5 x 10⁹/unit*</td>
</tr>
</tbody>
</table>

* methods validated for counting low numbers of leucocytes must be used.

NOTE: Visual inspection of platelet components for the swirling phenomenon, clumping, excessive red cell contamination and abnormal volume is a useful pre-issue check.

4.8.6 Transportation (for general guidelines see 3.10)
Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22°C ± 2°C with continuous gentle agitation.

4.9 Granulocytes, Apheresis

4.9.1 General Description
A component prepared from anticoagulated blood which is separated into components by a suitable apheresis machine with retention of granulocytes as the major cellular product suspended in a portion of the plasma. The remaining elements may be returned to the donor.

4.9.2 Technical Information

1. Granulocytes may be collected by a variety of apheresis systems using different protocols. Since yields may vary, each procedural protocol must be fully validated, documented and specifications set accordingly.

2. The component must not be agitated during storage.

3. The component must be irradiated before use.

4.9.3 Labelling (for general guidelines see 3.6)
The following shall be included on the label

- Granulocytes, apheresis and volume
- the producer's name in eye readable.
- the donation number
- the ABO group
- the RhD group stated as positive as negative
- the date of collection and expiry date and time
- the statement "Do not agitate"
- the temperature of storage

In addition, the following statements should be made:

CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

4.9.4 Storage (for general guidelines see 3.7)
Granulocytes, apheresis should be used as soon as possible after their preparation. Whether prepared in an open or closed system, if storage is unavoidable, the component should be stored at a core temperature of 22°C ± 2°C and used within 24 hours of collection.

4.9.5 Testing
1. In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, a minimum of 75% of those components tested for the parameters shown at 6.9.5.2 below shall meet the specified values.

2. Additional Test

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>10 per month or, if made less frequently, every component</td>
<td>Within locally defined nominal volume range</td>
</tr>
<tr>
<td>Total Granulocyte count</td>
<td></td>
<td>&gt; 10 x 10⁹ per unit</td>
</tr>
</tbody>
</table>

4.9.6 Transportation (for general guidelines see 3.10)

Containers for transporting granulocytes, apheresis should be equilibrated at room temperature before use. During transportation the temperature of the component must be kept as close as possible to the recommended storage temperature and on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22°C ± 2°C.

4.10 Fresh frozen plasma

4.10.1 General Description

Fresh frozen plasma is plasma that has been obtained from whole blood or by apheresis from a donor who has given at least one mandatory microbiological screen negative donation in the past 6-24 months and who otherwise meets the component release criteria. The plasma is rapidly frozen to a temperature that will maintain the activity of labile coagulation factors.

4.10.2 Technical Information

1. Ideally the plasma should be separated at 22°C ± 2°C before the red cell component is cooled to its storage temperature.

2. The method of preparation should ensure the component has the maximum level of labile coagulation factors with minimum cellular contamination.

3. A rapid freezing process should be used to ensure that a core temperature of 30°C or below is achieved within 2 hours of commencing the freezing process.

4. The maximum time period from venepuncture to obtaining a core temperature of -30°C or below is normally 8 hours.
4.10.3 Labelling (for general guidelines see 3.6)

The following shall be included on the label

- fresh frozen plasma and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number
- the ABO group
- the RhD group stated as positive or negative
- the date of preparation and expiry date of the frozen component
- the temperature of storage
- a warning that the component must be used within 4 hours of thawing

In addition, the following statements should be made:

CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

4.10.4 Storage (for general guidelines see 3.7)

1. Fresh frozen plasma should be stored at a core temperature of -30°C or below for a maximum of 12 months.

2. Although a storage temperature below -30°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.

3. Once thawed, fresh frozen plasma must not be refrozen and should be used immediately. If delay is unavoidable, the component should be stored at ambient temperature and used within 4 hours.

4.10.5 Testing

1. In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, a minimum of 75% of those components tested for the parameters shown at 4.10.5.2 below shall meet the specified values.

2. Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1%</td>
<td>≥150ml and within locally defined nominal volume range</td>
</tr>
<tr>
<td>Platelets</td>
<td>1%</td>
<td>&lt;30 x 10^7/1*</td>
</tr>
<tr>
<td>Factor VIIIc</td>
<td>1%</td>
<td>&gt;0.7 IU/ml</td>
</tr>
</tbody>
</table>
4.10.6  Transportation (for general guidelines see 3.10)

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straight away it should be transferred immediately to storage at the recommended temperature.

4.11  Cryoprecipitate

4.11.1  General Description

The component contains the major portion of Factor VIII, and von Willebrand factor, fibrinogen, Factor XIII and fibronectin from a unit of fresh frozen plasma. The plasma must be derived from a donor who has given at least one mandatory microbiological screen negative donation in the last 6-24 months and who otherwise meets the component release criteria.

4.11.2  Technical Information

1.  Cryoprecipitate is the cryoglobulin fraction of plasma obtained by thawing a single donation of fresh frozen plasma at 4°C ± 2°C.

2.  After preparation cryoprecipitate should be used immediately or rapidly frozen to a core temperature of -30°C or below within 2 hours of preparation.

4.11.3  Labelling (for general guidelines see 3.6)

The following shall be included on the component label

- cryoprecipitate and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number
- the ABO group
- the RhD group stated as positive or negative
- the date of preparation and expiry date of the frozen component
- the temperature of storage
- a warning that the component must be used within 4 hours of thawing

In addition, the following statements should be made:

CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

4.11.4  Storage (for general guidelines see 3.7)

1.  Cryoprecipitate should be stored at a core temperature of -30°C or below for a maximum of 12 months.
2. Although a storage temperature below -30°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.

3. Once thawed, cryoprecipitate must not be refrozen and should be used, immediately. If delay is unavoidable, the component should be stored at ambient temperature and used within 4 hours.

4.11.5 Testing

1. In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, a minimum of 75% of those components tested for the parameters shown at 4.11.5.2 below shall meet the specified values.

2. Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1%</td>
<td>Within locally defined nominal volume range</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>1%</td>
<td>&gt; 140 mg/unit</td>
</tr>
<tr>
<td>Factor VIIIc</td>
<td>1%</td>
<td>&gt; 70 iu/unit</td>
</tr>
</tbody>
</table>

4.11.6 Transportation (for general guidelines see 3.10)

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straight away it should be transferred immediately to storage at the recommended temperature.

4.12 Cryosupernatant Plasma

4.12.1 General Description

The supernatant plasma removed during the preparation of cryoprecipitate. The plasma must be derived from a donor who has given at least one mandatory microbiological screen negative donation in the past 6-24 months and who otherwise meets the component release criteria.

4.12.2 Technical Information

Plasma, cryoprecipitate depleted should be frozen to a core temperature of -30°C or below within 2 hours of separation from its cryoprecipitate.

4.12.3 Labelling (for general guidelines see 3.6)

The following shall be included on the component label

- Plasma, cryoprecipitate depleted and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number
- the ABO group
- the RhD group stated as positive or negative
- the date of preparation and expiry date of the frozen component
- the temperature of storage
- a warning that the component must be used within 4 hours of thawing

In addition, the following statements should be made:

**CAUTION**
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

4.12.4 Storage (for general guidelines see 3.7)

1. Plasma, cryoprecipitate depleted should be stored at a core temperature of -30°C or below for a maximum of 12 months.

2. Although a storage temperature below -30°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.

3. Once thawed, plasma cryoprecipitate depleted must not be refrozen and should be used immediately. If delay is unavoidable, the component should be stored at ambient temperature and used within 4 hours.

4.12.5 Testing

1. In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, a minimum of 75% of those components tested for the parameters shown at 4.12.5.2 below shall meet the specified value.

2. Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1%</td>
<td>Within locally defined nominal volume range</td>
</tr>
</tbody>
</table>

4.12.6 Transportation (for general guidelines see 3.10)

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straight away it should be transferred immediately to storage at the recommended temperature.

4.13 Components for Neonatal Use

4.13.1 General Description

1. It is good practice to provide neonates with components of lower volume by dividing standard components into sub batches. This minimises wastage of valuable components and provides the potential to reduce donor exposures.
However, provided they meet the specifications outlined below, blood components already specified in this Chapter are suitable for neonatal use.

2. When a component is divided for neonatal use, each sub batch must be identified by a unique number to ensure all sub batches of a component can be accounted for.

3. When a component is to be divided for neonatal use the index pack must first be mixed thoroughly by a validated procedure to ensure that the contents are homogeneous.

4. When components for neonatal use are prepared by dividing standard components the specifications shown in 4.13 shall apply.

4.13.2 Red Cells for IUT

1. General Description

A component for intrauterine transfusion, prepared by removing a proportion of the plasma from fresh whole blood.

2. Technical Information

(i) The component must be prepared and used within 5 days of collection (i.e. day 0) and should be free from clinically significant irregular blood group antibodies including high titre anti-A and anti-B (see Annex 3).

(ii) The component must be gamma irradiated and should be transfused within 24 hours of irradiation.

(iii) The component should be anti-CMV negative or leucocyte depleted and, unless the Blood Transfusion Centre recommends screening is unnecessary, should be Haemoglobin S screen negative.

(iv) Red Cells for IUT should be transfused through a standard screen filter.

3. Labelling Requirements (for general guidelines, see 3.6)

The following shall be included on the label

- red cells for IUT and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number and, if divided, sub batch number
- the ABO group
- the RhD group stated as positive or negative
- reference may also be made to other blood group information
- the composition of the anticoagulant solution
- the date of collection any expiry date and time
- the temperature of storage
- In addition, the following statements should be made:
CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

4. Storage (for general guidelines see 3.7)

(i) Red cells for IUT may be stored for a maximum of 5 days (from venepuncture i.e. day 0) at a core temperature of 4°C ± 2°C and should be used within 24 hours of irradiation.

(ii) Red cells for IUT prepared by an open procedure should be used as soon as possible. If storage is unavoidable, the component should be stored at a core temperature of 4°C±2°C and used within 24 hours of commencing the open process.

(iii) Variation from the core temperature of 4°C ± 2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.

(iv) Exceptionally, i.e. due to equipment failure at BTC, red cells for IUT which has been prepared by a closed system and exposed to core temperature not exceeding 10°C and not less than 1°C may be released for transfusion provided:

• that the component has been exposed to such a temperature change on one occasion only
• that the duration of the temperature change has not exceeded 5 hours.
• that a documented system is available in each BTC to cover such eventualities
• that adequate records of the incident are compiled and retained

5. Testing

(i) In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, red cells for IUT shall be free from clinically significant irregular blood group antibodies and high titre anti-A and/or anti-B. Furthermore, a minimum of 75% of those components tested for the parameters shown at 4.14.2.5.ii below shall meet the specified values.
(ii) Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1% or 10 per month whichever is greater If less than 10 per month, every component</td>
<td>Within locally defined nominal volume range</td>
</tr>
<tr>
<td>Haematocrit</td>
<td></td>
<td>Within local specification</td>
</tr>
</tbody>
</table>
6. Transportation (for general guidelines see 3.10)

The air temperature of transport containers for units of red cells for IUT should be maintained between 2°C and 10°C during transportation from the ETC to the place that they are intended for use. Transport time under these conditions normally should not exceed 12 hours.

4.13.3 Red Cells For Exchange Transfusion.

1. General Description

A component for exchange transfusion of neonates prepared by removing a proportion of the plasma from fresh whole blood.

2. Technical Information

i) The component must be prepared and used within 5 days of collection (i.e. day 0) and should be free from clinically significant irregular blood group antibodies including high titre anti-A and anti-B (see Annex 3).

ii) If required, the component should be anti-CMV negative or leucocyte depleted and unless the Blood Transfusion Centre recommends screening is unnecessary, should be Haemoglobin S screen negative.

iii) In certain circumstances (e.g. previous IUT) the component should be gamma irradiated and transfused within 24 hours of irradiation (see BCSH Guidelines). Centres may find it more convenient to irradiate all such components.

3. Labelling (For general guidelines, see 3.6)

The following shall be included on the label

- red cells for exchange transfusion and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number and, if divided, sub batch number
- the ABO group
- the RhD group stated as positive or negative
- reference may also be made to other blood group information
- the composition of the anticoagulant solution
- the date of collection and expiry date and time
- the temperature of storage

In addition the following statements should be made:

CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information
4. Storage (for general guidelines see 3.7)

i) Red cells for exchange transfusion may be stored for a maximum of 5 days (from venepuncture i.e. day 0) at a core temperature of 4°C ± 2°C.

ii) Red cells for exchange transfusion should be used within 24 hours of irradiation.

iii) Red cells for exchange transfusion prepared by an open procedure should be used as soon as possible. If storage is unavoidable, the component should be stored at a core temperature of 4°C ± 2°C and used within 24 hours of commencing the open process.

iv) Variation from the core temperature of 4°C ± 2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.

v) Exceptionally, i.e. due to equipment failure at a BTC, red cells for exchange transfusion which has been prepared in a closed system and exposed to a core temperature not exceeding 10° C and not less than 1° C may be released for transfusion provided:

• that the component has been exposed to such a temperature change on one occasion only.
• that the duration of the temperature change has not exceeded 5 hours
• that a documented system is available in each BTC to cover such eventualities
• that adequate records of the incident are compiled and retained.

vi) If red cells for exchange transfusion are unused within their specified shelf life they may be returned to stock provided:

• they are appropriately relabelled as red cells and "irradiated" (i.e. not for neonatal use).

• that the storage restrictions of irradiated red cells are observed i.e. use within 14 days of irradiation.

5. Testing

i) In addition to mandatory and other tests required for blood donations and which are described in annex 3 red cells for exchange transfusion shall be free from clinically significant irregular blood group antibodies and high titer anti-A and/or anti-B. Furthermore, a minimum of 75% of those components tested for the parameters shown at 4.13.4.5.ii below shall meet the specified values.
II) Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1% or 10 per month whichever is greater if less than 10 per month every component</td>
<td>Within locally defined nominal volume range</td>
</tr>
<tr>
<td>Haematocrit</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

6. Transportation (for general guidelines see 3.10)

The air temperature of transport containers for units of red cells for exchange transfusion should be maintained between 2° C and 10° C during transportation from the BTC to the place that they are intended for use. Transport time under these conditions normally should not exceed 12 hours.

4.13.4 Whole Blood for Neonatal Use

1. General Description

A unit of blood collected into an anticoagulant, and which subsequently may be divided into approximately equal volumes in a closed system. The component is otherwise not further processed.

Whole blood for neonatal use from which certain cellular or plasma elements have been removed as an operational expedient rather than for a specific clinical indication can be labelled as whole blood for neonatal use provided it meets the specification given at 4.13.4.5.

2. Technical Information

i) For exchange and massive transfusion of neonates, whole blood should be less than 5 days old.

ii) Whole Blood for Neonatal Use should be gamma irradiated before use and should be used within 24 hours of irradiation.

3. Labelling (for general guidelines see 3.6)

The following shall be included on the label

- Whole blood for neonatal use and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number and if divided, sub batch number
- the ABO group
- the RhD group stated as positive or negative
- the date of collection and expiry date
- the temperature of storage
  In addition, the following statements should be made:

CAUTION
Always check patient/component compatibility
Do not use of there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

4. Storage (for general guidelines see 3.7)

i) Whole blood for "top up" transfusion of neonates may be stored for a maximum of 35 days at a core temperature of 4°C ± 2°C if an adenine supplemented anticoagulant is used, otherwise maximum period of storage is 28 days at a core temperature of 4°C ±2°C.

ii) Whole blood for exchange or massive transfusion of neonates should be used within 5 days of venepuncture.

iii) Variation from the core temperature of 4°C ± 2°C must be kept to a minimum during storage and restricted to any short period necessary of examining, labelling or issuing the component.

iv) Exceptionally, i.e. due to equipment failure at a BTC, whole blood for neonatal use which has been prepared in a closed system exposed to a core temperature not exceeding 10°C and not less than 1°C may be released for transfusion provided:

   • that the component has been exposed to such a temperature change on one occasion only
   • that the duration of the temperature change has not exceeded 5 hours
   • that a documented system is available in each BTC to cover such eventualities
   • that adequate records of the incident are compiled and retained.

5. Testing

i) In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, whole blood for neonatal use shall be free from clinically significant irregular blood group antibodies and high titer anti-A and/or anti-B. Furthermore, a minimum of 75% of those components tested for the parameters shown at 4.13.5II below shall meet the specified values.

ii) Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1% or 10 per month whichever is is greater if less than 10 per month, every component</td>
<td>Within locally defined nominal volume range</td>
</tr>
</tbody>
</table>
6. Transportation (for general guidelines see 3.10)
The air temperature of transport containers for units of whole blood for neonatal use should be maintained between 2°C and 10°C during transportation from the BTC to the place that they are intended for use. Transport time under these conditions normally should not exceed 12 hours.

4.13.5. Red Cells, Plasma Reduced for Neonatal Use.

1. General Description

A component prepared by removing approximately 100-150ml of plasma from a unit of whole blood. A closed system may be used to divide the remaining elements into approximately equal volumes.

2. Technical Information.

i) The volume of remaining plasma will influence the haematocrit of the component.

ii) If intended for exchange or massive transfusion the component should be irradiated before use and should be used within 24 hours of irradiation.

3. Labelling (for general guidelines see 5.6)

The following shall be included on the label

- red cells, plasma reduced for neonatal use and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number and, if divided, sub batch number
- the ABO group
- the RhD group stated as positive or negative
- the composition of the anticoagulant solution
- the date of collection and expiry date
- the temperature of storage

In addition, the following statements should be made

CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

4. Storage (for general guidelines see 3.7)

i) Red cells, plasma reduced for top up transfusion of neonates may be stored for a maximum of 35 days at a core temperature of 4°C ± 2°C if an adenine supplemented anticoagulant is used otherwise the maximum period of storage is 28 days at a core temperature of 4°C ± 2°C.
ii) Red cells, plasma reduced for exchange or massive transfusion of neonates should be used within 5 days of venpuncture. (See also 4.13.3 red cells for exchange transfusion).

iii) Variation from the core temperature of $4^\circ C \pm 2^\circ C$ must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.

iv) Exceptionally, i.e. due to equipment failure at a BTC, red cells plasma reduced for neonatal use which has been prepared in a closed system and exposed to a core temperature not exceeding $10^\circ C$ and not less than $1^\circ C$ may be released for transfusion provided:

- that the component has been exposed to such a temperature change on one occasion only.
- that the duration of the temperature change has not exceeded 5 hours.
- that a documented system is available in each BTC to cover such eventualities
- that adequate records of the incident are compiled and retained

Testing

i) In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, red cells, plasma reduced for neonatal use shall be free from clinically significant irregular blood group antibodies and high titre anti-A and/or anti-B. Furthermore, a minimum of 75% of those components tested for the parameters shown at 4.13.5.II, below shall meet the specified values.

ii) Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1% or 10 per month whichever is greater if less than 10 per month, every component</td>
<td>Within locally defined nominal volume range</td>
</tr>
<tr>
<td>Haematocrit</td>
<td></td>
<td>0.50-0.70</td>
</tr>
</tbody>
</table>

6. Transportation (for general guidelines see 3.10)

The air temperature of transport containers for units of red cells, plasma reduced for neonatal use should be maintained between $2^\circ C$ and $10^\circ C$ during transportation from the BTC to the place that they are intended for use. Transport time under these conditions normally should not exceed 12 hours.
4.13.6. Red Cells in Additive Solution, for Neonatal Use.

1. General Description.

A component prepared by removing most of plasma from whole blood. The red cells are suspended in an additive solution and, using a closed system, may be divided into approximately equal volumes.

2. Technical Information.

i) The volume of remaining plasma will influence the haematocrit of the component.

ii) This component is not suitable for exchange or massive neonatal transfusion.

3. Labelling (for general guidelines see 3.6) The following shall be included on the label.

- red cells in additive solution, for neonatal use and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number and, if divided, sub batch number
- the ABO group
- the RhD group stated as positive or negative
- the composition of the additive solution
- the date of collection and expiry date
- the temperature of storage

In addition, the following statements should be made:

CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

4. Storage (for general guidelines see 3.7)

i) Red cells in additive solution for top up transfusion of neonates may be stored for a maximum of 35 days at a core temperature of 4°C ± 2°C.

ii) Variation from the core temperature of 4°C ± 2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling, or issuing the component.

iii) Exceptionally, i.e. due to equipment failure at a BTC red cells in additive solution, for neonatal use -which has been prepared in a closed system and exposed to a core temperature not exceeding 10°C and not less than 1°C may be released for transfusion provided:

- that the component has been exposed to such a temperature change on one occasion only
- that the duration of the temperature change has not exceeded 5 hours
- that a documented system is available in each BTC to cover such eventualities
- that adequate records of the incident are compiled and retained
5. Testing

i) In addition to the mandatory and other tests required for blood donations and which are described in annex 3, a minimum of 75% of those components tested for the parameters shown at 4.13.6.5.ii below shall meet the specified values.

ii) Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1% or 10 per month whichever is greater if less than 10 per month, every component</td>
<td>Within locally defined nominal volume range</td>
</tr>
<tr>
<td>Haematocrit</td>
<td></td>
<td>0.50 - 0.70</td>
</tr>
</tbody>
</table>

Transportation (for general guidelines see 3.10)

The air temperature of transport containers for unit of red cells in additive solution for neonatal use should be maintained between 2°C and 10°C during transportation from the BTC to the place that they are intended for use. Transport time under these conditions normally should not exceed 12 hours.

4.13.7. Red Cells Plasma Reduced, Leucocyte Depleted For Neonatal Use.

1. General Description.

A plasma reduced component for neonatal use containing less than $5 \times 10^6$ leucocytes.

2. Technical Information.

i) The volume of remaining plasma will influence the haematocrit of the component.

ii) Leucocyte depletion can be achieved by a number of methods which should be validated before use.

iii) If filtration is used the capacity of the filter should not be exceeded.

iv) Leucocyte depletion procedures should not reduce red cell volume by more than 15%.

v) Using a closed system the remaining elements may be divided into approximately equal volumes.

vi) If the leucodepletion process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct donation number is put on the final component pack.

3. Labelling (for general guidelines see 3.6)

The following shall be included on the label:

- red cells plasma reduced, leucocyte depleted for neonatal used and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number and, if divided, sub batch number
- the ABO group
- the RhD group stated as positive or negative
- the composition of the anticoagulant solution
- the date of collection and expiry date
- the temperature of storage.

In addition, the following statements should be made:

CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

Storage (for general guidelines see 3.7)

i) Red cells plasma reduced leucocyte depleted for top up transfusion of neonates may be stored for a maximum of 35 days at a core temperature of 4°C ± 2°C if an adenine supplemented anticoagulant is used otherwise the maximum period of storage is 28 days at a core temperature of 4°C ± 2°C.

ii) Red cells plasma reduced leucocyte depleted for exchange or massive transfusion of neonates should be used, within 5 days of venepuncture.

jii) Variation from the core temperature of 4°C ± 2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.

iv) Exceptionally i.e. due to equipment failure at a BTC, red cells plasma reduced leucocyte depleted for neonatal use which has been prepared in a closed system and exposed to a core temperature not exceeding 10°C and not less than 1°C may be released for transfusion provided:

- that the component has been exposed to such a temperature change on one occasion only.
- that the duration of the temperature change has not exceeded 5 hours
- that a documented system is available in each BTC to cover such eventualities
- that adequate records of the incident are compiled and retained.

Testing

(i) In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, the manufacturer must ensure (e.g. by a recognized process control methodology or by performing leucocyte counts on all components) that leucocyte depleted components meet their specification before they are released to stock as "leucocyte depleted". In addition, the component shall be free from clinically significant irregular blood group antibodies and high titre anti-A and/or anti-B. Furthermore, a minimum of 75% of those components tested for the other parameters shown at 4.13.7.5.ii below shall meet the specified values.
(ii) Additional Tests

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1% or 10 per month whichever is greater</td>
<td>Within locally defined nominal volume range</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>If less than 10 per month, every component</td>
<td>0.50 - 0.70</td>
</tr>
<tr>
<td>Leucocyte count*</td>
<td>As per 4.13.7.5.i</td>
<td>&lt; 5x 10⁷/donation</td>
</tr>
</tbody>
</table>

*methods validated for counting low numbers of leucocytes must be used
6. Transportation (for general guidelines see 5.7)

The air temperature of transport containers for units of red cell plasma reduced, leucocyte depleted for neonatal use should be maintained between 2°C an 10°C during transportation from the BTC to the place that they are intended for use. Transport time under these conditions normally should not exceed 12 hours.

4.13.8 Red Cells in Additive Solution Leucocyte Depleted, for Neonatal use

1. General Description

A component for neonatal use containing less than 5x10^6 leucocytes. The red cells are suspended in an additive solution and may be divided into approximately equal volumes using a closed system.

2. Technical Information

(i) The volume of remaining plasma will influence the haematocrit of the component.

(ii) Leucocyte depletion can be achieved by a number of methods which should be validated before use.

(iii) If filtration is used the capacity of the filter should not be exceeded.

(iv) Leucocyte depletion procedures should not reduce red cell volume by more than 15%.

(v) Using a closed system the remaining elements may be divided into approximately equal volumes.

(vi) If the leucodepletion process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct donation number is put on the final component pack.

(vii) This component is not suitable for exchange or massive neonatal transfusion.

3. Labelling (for general guidelines see 3.6) The following shall be included on the label

- red cells in additive solution leucocyte depleted for neonatal use and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number and, if divided, sub batch number
- the ABO group
- the RhD group stated as positive or negative
- the composition of the additive solution
- the date of collection and expiry date
- the temperature of storage
In addition, the following statements should be made:

CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information

Storage (for general guidelines see 3.7)

i) Red cells in additive solution leucocyte depleted for top up transfusion of neonates may be stored for a maximum of 35 days at a core temperature of 4°C ± 2°C.

ii) Variation from the core temperature of 4°C ± 2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.

iii) Exceptionally i.e. due to equipment failure at a BTC, red cells in additive solution leucocyte depleted for neonatal use which has been prepared in a closed system and exposed to a core temperature not exceeding 10°C and not less than 1°C may be released for transfusion provided:

- that the component has been exposed to such a temperature change on one occasion only
- that the duration of the temperature change has not exceeded 5 hours
- that a documented system is available in each BTC to cover such eventualities
- that adequate records of the incident are compiled and retained.

Testing

i) In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, the manufacturer must ensure (e.g. by a recognized process control methodology or by performing leucocyte counts on all components) that leucocyte depleted components meet their specification before they are released to stock as "leucocyte depleted". Furthermore, a minimum of 75% of those components tested for the other parameters shown at 4.13.8.5. ii below shall meet the specified values.

ii) Additional Tests.

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1% or 10 per month whichever is greater If less than 10 per month, every component</td>
<td>Within locally defined nominal volume range 0.50-0.70</td>
</tr>
<tr>
<td>Haematocrit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leucocyte count*</td>
<td>Asper4.13.8.5.i</td>
<td>5x10^6/donation</td>
</tr>
</tbody>
</table>

*Methods validated for counting low numbers of leucocytes must be used
6. Transportation (for general guidelines see 3.10)

The air temperature of transport containers for units of red cells in additive solution, leucocyte depleting for neonatal use should be maintained between 2°C and 10°C during transportation from the ETC to the place that they are intended for use. Transport time under these conditions normally should not exceed 12 hours.

4.13.9. Fresh Frozen Plasma for Neonatal Use

1. General Description.

Fresh frozen plasma for neonatal use is plasma that has been obtained from whole blood or by apheresis.

Using a closed system the component may be sub-divided into approximately equal volumes and rapidly frozen to a temperature that will maintain the activity of labile coagulation factors.

2. Technical Information.

i) The plasma must be derived from a donor who has given at least one mandatory microbiological screen negative donation in the last 6-24 months.

ii) Ideally the plasma should be separated at 22°C±2°C before the red cell component is cooled to its storage temperature.

iii) The method of preparation should ensure the component has the maximum level of labile coagulation factors with minimum cellular contamination.

iv) A rapid freezing process should be used to ensure that a core temperature of -30°C or below is achieved within 2 hours of commencing the freezing process.

v) The maximum time period from venepuncture to obtaining a core temperature of -30°C or below is normally 8 hours.

3. Labelling (for general guidelines see 3.6)

The following shall be included on the label:

- fresh frozen plasma for neonatal use and volume
- the producer's name in eye readable and BTS approved barcode format
- the donation number and, if divided, sub batch number
- the ABO group
- the RhD group stated as positive or negative
- the date of preparation and expiry date of the frozen component
- the temperature of storage
- a warning that the component should be used within 4 hours of thawing.

In addition, the following statements should be made:
CAUTION
Always check patient/component compatibility
Do not use if there are signs of deterioration or damage
Use a standard transfusion set
Risk of adverse reaction/infection
Please contact your blood bank/BTC for further information.

4. Storage (for general guidelines see 3.7)

i) Fresh frozen plasma for neonatal use should be stored at a core temperature of \( \leq 30^\circ\text{C} \) or below for a maximum of 12 months.

ii) Although a storage temperature below \(-30^\circ\text{C}\) improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.

iii) Once thawed, fresh frozen plasma for neonatal use must not be refrozen and should be used immediately. If delay is unavoidable, the component should be stored at ambient temperature and used within 4 hours.

Testing
In addition to the mandatory and other tests required for blood donations and which are described in Annex 3, fresh frozen plasma for neonatal use shall be free from clinically significant irregular blood group antibodies and high titer anti-A and/or anti-B. Furthermore, a minimum of 75% of those units components tested for the parameters shown at 4.13.9.5.ii below shall meet the specified values.

ii) Additional Tests.

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>FREQUENCY OF TEST</th>
<th>SPECIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1% or 10 per month whichever is greater If less than 10 per</td>
<td>Within locally defined nominal volume range</td>
</tr>
<tr>
<td>Platelets</td>
<td></td>
<td>(&lt;30\times10^9/\text{l})*</td>
</tr>
<tr>
<td>Factor VIIIc</td>
<td></td>
<td>(&gt;0.7\text{iu/ml})</td>
</tr>
</tbody>
</table>

* prefreeze

6. Transportation (for general guidelines see 3.10)

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straight away it should be transfused immediately to storage at the recommended temperature.

4.14 Irradiated Components.

This section provides guidance on the irradiation of components in the knowledge that this is an evolving scientific area where further developments are envisaged.
It is not necessary to irradiate the following components: cryopreserved red cells after washing fresh frozen plasma, cryoprecipitate or fractionated plasma products.

Irradiated components not used for the intended recipient can safely be used for recipients who do not require irradiated components provided the requirements of 3.7 and 3.9 have been satisfied. However, any reduction in shelf life resulting from the irradiation process must be observed.

Irradiated components should conform to their appropriate specification previously given in this Chapter. In addition guidelines shown below should be observed.

4.14.1 Description

Irradiated components are components that have been irradiated by a validated procedure.

4.14.2 Technical Information

1. Other than for use in IUT or exchange transfusion, red cell can be irradiated at any time up to 14 days after collection.

2. Red cells for use in IUT or exchange transfusion, should be transfused within 24 hours of irradiation and, in any event, should be used within 5 days of collection.

3. Platelets can be irradiated at any stage in their 5 day storage.

4. Granulocytes should be irradiated as soon as possible after production.

5. For red cells, platelets and granulocytes the recommended minimum dose achieved in the irradiation field is 25Gy, with no part receiving >50Gy.

6. Platelets to be transfused in utero to treat alloimmune thrombocytopenia must be irradiated.

7. Laboratories performing irradiation of blood components must work to a clearly defined specification and are strongly recommended to work closely with a medical physicist. The defined irradiation procedure must be validated and there must be regular monitoring of the blood component dosimetry and the laboratory equipment.

8. It is recommended that irradiation of blood components is carried out using dedicated blood irradiation machines. If radiotherapy machines are used, equivalent protocols should be developed.

9. Gamma ray sensitive labels should be used as an aid to differentiating irradiated from non-irradiated components. However, it may not be necessary to attach a gamma ray sensitive label to every component pack provided that the irradiation procedure follows a validated, documented and well controlled system of work that is integrated to the component labelling and release mechanism and permits retrospective audit of each stage of the irradiation process.
10. There should be a permanent record of all units irradiated. This should include details of irradiation batch and donation numbers, component type, the site of irradiation, when irradiation was performed and by whom.

4.14.3 Labelling

1. Irradiated components must be identified by an approved overstick label. The label should be permanent and include the date of irradiation and any reduction in shelf life. Approved barcode labels should be used.

Labels which are sensitive to gamma rays and change from "NOT IRRADIATED" to "IRRADIATED" are available and are considered a useful indicator of exposure to gamma rays. The dose at which the label change to "IRRADIATED" must be marked on the label. It must be remembered that such labels simply reflect that the unit has been exposed to gamma rays and their use does not replace the need for regular and precise dosimetry nor carefully controlled working procedures.

4.14.4. Storage

1. Red cell components can be stored for up to 14 days after irradiation.

2. Where irradiated red cells are intended for intra uterine or exchange transfusion or where the patient is at particular risk from hyperkalaemia, red cells should be transfused within 24 hours of irradiation. Furthermore, red cells intended for IUT or exchange transfusion should be transfused within 5 days of collection.

3. Irradiated platelets can be stored up to their normal shelf life of 5 days after collection, and granulocyte components should be irradiated and used as soon as possible after their preparation but within the shelf life specified earlier in this Chapter.

4. Granulocytes should be transfused with minimum delay after irradiation.
Annex 1

General Specifications for Blood Donor Sessions

1. Donor Identification

1.1 Before the venepuncture the donor must be positively identified and BTC procedures followed to check this action. The identically numbered labels must be checked to ensure that those on the blood packs, sample tubes and donation records are identical.

2. Haemoglobin or Haematocrit Screening

2.1 Copper sulphate haemoglobin screen

Aqueous copper sulphate, coloured blue, with a specific gravity of 1.053, equivalent to 125g/1 haemoglobin is normally used to test female donors. Copper sulphate, coloured green, with a specific gravity of 1.055, equivalent to 135g/1 can be used to test male donors. These stock solutions should be colour-coded and labelled accordingly.

2.2 Copper sulphate storage

Stock solutions should be stored at room temperature in tightly capped, dark glass containers to prevent evaporation and contamination. Copper sulphate solutions must not be frozen or exposed to high temperatures. The specific gravity of each batch in the stock solution should be checked at least weekly by designated staff with a calibrated hydrometer. The date, the result and the name of the individual who carried out the check, must be recorded on the bottle.

2.3 Copper sulphate for routine use

Designated staff should be responsible for dispensing the stock solutions for sessional use. The solution shall be mixed before dispensing the required amount of each solution into appropriately labelled clean dry tubes or bottles. These solutions shall be changed daily or after 25 tests, depending on the volume of solution dispensed (normally 25 mis), otherwise contamination of the solution will affect the accuracy of the test. Any used solution at the end of a session shall be discarded. The calibration temperature of the copper sulphate should be that specified by the manufacturer to provide the correct specific gravity, e.g. cupric sulphate MAR, (material conforming to the AnalalR specification) has the correct specific gravity for Hb estimation at 15.5°C.

2.4 Copper sulphate procedure: fingerprick blood sample

2.4.1 The skin at the chosen site on the finger must be cleaned with antiseptic solution and wiped clean with sterile gauze or cotton wool. The skin must be punctured firmly, near the end but slightly to the side of the finger, with a sterile disposable lancet, or spring loaded disposable needle system. A good free flow of blood must be obtained.
2.4.2 The first drop of blood should be discarded and the finger should not be squeezed repeatedly as this may dilute the blood with tissue fluid and give falsely low results.

2.4.3 Blood from ear lobe puncture should not be used as it has a higher haemoglobin and haematocrit than blood from a finger prick sample and may allow donors with unsuitably low levels to give blood.

2.4.4 The blood is collected into capillary tube without any air entry as this may prevent or delay the delivery of the drop.

2.4.5 One drop of blood is allowed to fall by unassisted gravity from the tube from a height of 1 cm above the surface of the copper sulphate solution. The drop is observed for 15 seconds. If the drop of blood has a higher specific gravity than the solution, it will sink within 15 seconds. If not, the sinking drop will hesitate, remain suspended, or rise to the top of the solution.

2.4.6 Results are recorded as pass or fail.

2.5 Spectrophotometric method for haemoglobin screening

2.5.1 If a haemoglobin photometer is used to provide a quantitative measurement of haemoglobin at the donor session, standard operating procedures for the use of the instrument must be available in the session procedure manual.

2.5.2 They should include a technique whereby the performance of the photometer is validated by the regular use of appropriate calibration working standards.

2.6 The microhaematocrit centrifuge should be checked at a minimum of 6 months and preferably every 3 months by an appropriate qualified person using a precision RPM meter and a stop-watch to check speed, acceleration and retardation.

2.6.1 The microhaematocrit centrifuge should be calibrated when first placed in service, after repairs, and annually thereafter.

2.6.2 The time and speed should be checked at a minimum of 6 months and preferably every 3 months by an appropriate qualified person using a precision RPM meter and a stop-watch to check speed, acceleration qualification and retardation.

2.6.3 A calibration method that provides quality control and allows selection of optimal centrifugation time, is examination of replicate specimens or red cell suspensions within, below and above the acceptable haematocrit range.

2.6.4 The time selected for routine use should be the maximum time at which maximum packing occurs. Deviation of 2% between replicates is acceptable.

2.6.5 If a microhaematocrit method is employed for Hb screening, standard operating procedures for the use of this instrument must be available in the session procedure manual.
3. **Preparation of the Venepuncture Site**

3.1 Blood should be drawn from a suitable vein in the antecubital fossa in an area that is free of skin lesions. The veins can be made more prominent by using an inflated blood pressure cuff.

3.2 A prolonged cuff pressure of greater than 60mm Hg should not be employed as this could alter some blood constituents and reduce the quality of the blood collected, particularly with regard to the member of functional platelets obtained and Factor VIII recovery.

3.3 Although it is not possible to guarantee sterility of the skin surface for venepuncture, a strict standardized procedure for the preparation of the venepuncture site should be in operation to achieve surgical cleanliness and thus to provide maximum possible assurance of a sterile product.

3.4 The antiseptic solution used should be allowed to dry completely or wiped dry with sterile gauze before venepuncture and the prepared area must not be touched with fingers before the needle is inserted.

4. **Preparation of the Blood Pack**

4.1 The blood collection set must be in date and inspected for any defects. These may be hidden behind the label attached to the container so careful inspection is required.

4.2 Moisture on the surface of plastic pack after unpacking should arouse suspicion of a leak and if one or more packs in any packet is found to be abnormally damp, non of the packs in that container should be used.

4.3 The solution in the set should be checked for clarity and must be clear before accepting the packs for use.

4.4 The blood pack should be positioned below the level of the donor's arm and the blood collection tube must be clamped off;

4.5 The method used for monitoring the volume of blood removed should be checked to be in working order and the pack placed in the correct position for the method to be effective.

5. **Performance of the Venepuncture**

5.1 Venepuncture should only be undertaken by authorized and trained personnel according to the policy of the BTC.

5.2 If local anesthetic is used this should be a licensed medicinal product and injected in manner which avoids any chance of donor to donor cross infection (e.g. using individual disposable syringes and needles). A record of the batch number (s) should be made at each blood collection session and be capable of being related to individual donors.
5.3 Containers of local anesthetic should be inspected for any leakage and if glass, inspected for cracks. Any suspect containers should be rejected.

5.4 Unused material should be discarded at the end of each donor session.

5.5 An aseptic technique must be used for drawing up the local anesthetic into the syringe and the needle changed prior to the injection of the local anesthetic.

5.6 Items used for venepuncture should be obtained in a sterile, single use disposable form. If the dry outer wrapping of sterile packs becomes wet the contents must not be used. Containers of bulk sterilized items should be labelled and dated when they were sterilized and when opened. Unopened sterilized containers may be stored for 2 or 3 weeks provided the outer package is sealed.

5.7 Prior to use, sessional staff must ensure that the materials used for venepuncture are sterile, in date and suitable for the procedure to be undertaken. The sterile donor needles should not be uncovered and its tamperproof cover checked for integrity immediately prior to the venepuncture.

5.8 A soon as the venepuncture has been performed, the clamp on the bleed line must be released.

5.9 It is important that a clean skillful venepuncture is carried out to ensure the collection of a full, clot free unit of blood suitable for the preparation of labile blood components.

5.10 The tubing attached to the needle should be taped to hold the needle in place during the donation.

6. Blood Donation

6.1 If necessary, the donor should be asked to open and close his/her hand, over a suitable hand grip, slowly every 10-12 seconds to encourage a free flow of blood.

6.2 The donor should never be left unattended during or immediately after donation and should be kept under observation throughout the phlebotomy.

6.3 Blood anticoagulation

6.3.1 The blood and anticoagulant should be mixed gently and periodically (approximately every 30 seconds) during collection. Mixing should be achieved by manual inversion of the blood pack every 30 seconds, or automatically by placing the blood pack on a mechanical agitator or by using a rocking device.

6.4 Blood Flow

6.4.1 Blood flow should be constantly observed to ensure that the flow is uninterrupted. Local procedures should specify the maximum acceptable duration of collection times.
6.5 Blood Volume Monitoring

6.5.1 The volume of blood withdrawn must be controlled to protect the donor from excessive loss of blood and to maintain the correct proportion of anticoagulant to the blood.

6.5.2 The most efficient way of measuring the blood volume in plastic bags is by weight. The mean weight of 1ml of blood is 1.06g; a unit containing 405-495 ml should therefore weigh 430-525g plus the weight of the container and its anticoagulant.

6.5.3 If it is not possible to adjust the weighing device in use for the tare weight of the container and anticoagulant solution it is advisable to record the minimum and maximum weight for the brand of pack in use as products from different manufactures may vary considerably.

6.5.4 Several kinds of weighing equipment are available and such devices should be used according to the manufacturers' instructions for weighing blood into its plastic pack and periodically calibrated by appropriate techniques.

6.6 Sample Collection

6.6.1 At the end of the donation, the tubing can be temporarily clamped with a haemostat. The donor samples can then be collected by a method that precludes contamination of the donor unit. Any reusable equipment must be cleaned between donations, e.g. scissors and haemostat. The method employed must be clearly defined in the sessional procedures manual.

6.7 Completion of the Donation

6.7.1 The pressure cuff should be deflated and the needle then removed from the arm. Immediate pressure should then be applied to the venepuncture site with a sterile cotton wool ball or gauze.

6.7.2 The needle must be discarded into a special container designed to prevent any risk to personnel.

6.7.3 The bag should be inverted several times to mix the contents thoroughly.

6.7.4 The free end of the tubing should be sealed immediately. The blood contained in the collection tube should be expressed into the pack containing the blood donation and allowed to flow back into the tube to ensure anticoagulation.

The sealed off tubing left attached to the bag may be further sealed into segments for crossmatching purposes preferably using a heat sealer. If this is done the segment number must be clearly and completely readable on each segment and it must be possible to separate the segments from the container without compromising the sterility of the container.

6.7.5 The arm and general well-being of the donor should be checked.
6.8  Final Donation Inspection

6.8.1  All bag defects, e.g. pinhole leaks, must be recorded and all defects should be reported to the QA Manager. If the defect appears to be batch related, all packs and blood collected in them must be set aside for further investigation.

6.9  Safety Related Defects

6.9.1  Any safety related defects in equipment including single use items must be reported via the head of department to the DoH.

7.  Declaration of Health

7.1  Active steps must be taken regarding the medical history of donors to ensure compliance with the requirements listed in Chapter 1, paragraph 1.3 of this section.
Annex 2

Premises

1. General Considerations

1.1 Premises used for the preparation of components from blood and plasma will be subjected to scrutiny by the Drugs Control Authority. Such facilities must comply with the principles embodied in the current Guide to Good Pharmaceutical Manufacturing Practice (HMSO).

1.2 Notwithstanding the fact that premises used for mobile donor sessions may often be accepted, from necessity as the only local venue available, they must be of sufficient size, constructions and location to allow proper operation, cleaning and maintenance, in accordance with accepted rules of hygiene and in compliance with revised Requirements for Biological Substances No.1 (General Requirements for Manufacturing Establishments and Control Laboratories, WHO Technical Report Series No. 323 1966).

1.3 The designed person in charge of the blood collection team should in all cases be provided with a written plan of action appropriate to each venue. This can be used if conditions on arrival are not found to be acceptable. Care must be taken to avoid disturbances of any other activities within the venue if it is being shared.

2. Activities to be borne in mind when accepting a venue for mobile sessions

2.1 Registration of donors and all other necessary data processing. If possible, access to a telephone should be immediate, and certainly "on-site".

2.2 Laboratory and medical examination of donors as appropriate, to determine fitness to donate.

2.3 Withdrawal of blood from donors without risk of contamination and errors.

2.4 Performance of apheresis, where applicable, by single-arm techniques only. When apheresis machines are to be used, the environment should conform to the appropriate manufactures recommendations. Flooring should be non-slip, whether for a routine or an apheresis session.

2.5 Social and medical care of donors, including those who suffer reactions. Sufficient seating should be provided for donors and staff, with allowances made for possible queues during busy periods.

2.6 Storage of equipment, reagents and disposals.

2.7 Storage during the session of blood and components if they are not to be transferred immediately to the BTC or to appropriate storage in the team vehicle.
2.8 Access to an adequate electrical supply for any on-board refrigerator of the sessional vehicle and for all electrical equipment used on the session.

2.9 The space required for these activities will obviously depend on the workload and rate.

3. **Health and safety factors to be considered**

   3.1 The requirement of the Health and Safety at Work Act should be taken into account when selecting sessional venues. Premises should be safe, clean and comfortable for donors and staff.

   3.2 In particular, the following points should be borne in mind.

   3.2.1 The venue should be as close as possible to the centre of population being served. It should be possible for the sessional vehicle(s) to park in close proximity to the access doors to facilitate off-loading. The ground to be covered by staff carrying equipment should be even and well-lit. Preferably, the space to be used should not entail carriage of equipment on stairs. A similar safe approach should be ensured for donors, with as much provision as possible for the parking of their cars. Notices should be displayed, directing donors to the appropriate entry point of the building and to the room being used.

   3.2.2 Arrangement of furniture and equipment within the available space should be such as to minimise crowding (with its increased possibility of mistake or accident), enabling adequate supervision and ensuring a smooth and logical work-flow.

   3.2.3 Fire exits should be unobstructed and operational. All sessional staff must be aware of their location and that of the fire extinguishers.

   3.2.4 Lighting should be adequate for all the required activities. Provision must be made for the use of emergency lighting in the event of interruption of the electricity supply.

   3.2.5 Environmental control may not be within the power of mobile team, but every effort should be made to ensure that the space does not become too hot, too cold or stuffy. Subsidiary cooling fans and heating should be carried on sessional vehicles, and used as necessary. This equipment should be subjected to a planned maintenance programme at the BTC.

   3.2.6 Facilities for the provision of refreshments for donors and staff should be separated from the other activities of a donor session whenever possible. Every effort should be made to ensure that equipment used in this area poses the minimum threat of danger to all persons.

   3.2.7 Toilet facilities for male and female donors and staff should be provided. Separate washing facilities are desirable for those staff involved in "clean" procedure.

   3.2.8 Adequate facilities should be available for the disposal of waste. On mobile sessions, solid waste should be collected and contained in a suitable manner for return to the BTC and subsequent disposal.
Annex 3

Specifications for Laboratory Test Procedures

1. General considerations

1.1 Scope

These specifications provide guidance on the tests required for blood donations. Specific procedures should be written by individual BTCs in the form of Standard Operating Procedures.

1.2 Test Reagents, Kits and Equipment

1.2.1 Unless validated for alternative techniques, test kits and reagents should be stored and used according to the manufacturer's instructions.

1.2.2 All test procedures should be documented and an inventory maintained of kits and reagents in stock.

1.2.3 Procedures should ensure the traceability of the batch number and manufacturer of kits and reagents and, if relevant, the serial number of equipment used to test every donation.

1.2.4 Test equipment should be validated, calibrated and maintained. Appropriate records for these activities should be made and retained.

1.2.5 Appropriate reactivity with control samples must be demonstrated with every series of tests.

A series of tests is defined as the number of tests set up at the same time, under the same conditions and processed in a similar manner. Where a microplate format is used for microbiological testing, each plate constitutes a series even if only a few wells are used.

1.3 Reporting Results

1.3.1 The laboratory report should indicate the result of each and every test, preferably by a system that provides positive sample identification. Individual test results should be recorded either manually or ideally, by a computer.

1.3.2 Reporting a series of tests, particularly those of a microbiological nature, by an 'assumed negative' procedure is potentially dangerous and not acceptable.

1.4 Release of Tested Components

Standard procedures must ensure that blood and blood components can not be released for issue until all the required laboratory tests (mandatory and additional)
have been completed, documented and approved within a validated system of work. Compliance with this requirement may be achieved by:

1.4.1 The use of a computer programme, or suite of programmes, which requires the input of valid and acceptable test results for all the mandatory and required laboratory tests before permitting or withholding, the release of each individual unit.

1.4.2 Where a computer-based system is not used, a system which requires documented approval for the release of each individual unit by a designated person.

1.4.3 Where the computer-based system is temporarily unavailable, it is necessary to revert to the procedure in 1.4.2.

2. Mandatory Testing of Blood Donations

2.1 Blood Group Serology Tests (Mandatory)

2.1.1 ABO Blood Grouping

1. The ABO blood group shall be determined on each blood donation. The primary blood pack and any derived components for direct clinical use shall be labelled appropriately.

2. Where the ABO group of a donor has been determined previously within the Blood Transfusion Service and records of that assigned ABO group are available to the current testing centre, the determination of the ABO blood grouping by testing the plasma may be omitted.

3. For donors whose ABO blood group is unknown, e.g. a first time donor, the ABO blood group shall be determined by testing both the red cells and plasma of the donor with blood grouping reagents which comply with Section 2 of these Guidelines the ABO blood group would only be accepted when the results are in agreement.

4. There is no need to test with two different examples of ABO reagents if the reagents comply with Section 2 of these Guidelines.

   For those donors whose ABO group is known, a single test can be used provided this shows agreement with the previously recorded ABO blood group of the donor.

5. Quality Control of ABO Blood Grouping

   Quality control of procedures recommended by reagent and equipment manufacturers should be followed.

   Before a blood grouping reagent is used, appropriate reactivity with control cells should be confirmed.
6. The following minimum controls are required for each series of ABO blood grouping tests:-

For anti-A, anti-B, anti-AB and appropriate reactions must be obtained with A¹, A², B and O cells

Reagent red cell samples must give unequivocal appropriate reactions with anti-A; anti-B, anti-AB and/or anti-A+B.

Appropriate reactivity with control red cell samples expressing weak antigens (e.g. Ax) should also be confirmed regularly during use, although not necessary with each series of tests.

2.1.2 RhD Grouping

1. The RhD blood group shall be determined on each donation of blood. The primary blood pack and any derived components for direct clinical use shall be labelled appropriately.

2. The RhD blood group shall be determined by testing the red cells of the donor with anti-D blood grouping reagents which comply with Section 2 of these guidelines.

The reactivity of particular partial D (D variant) cells in blood grouping procedures depends on the methodology and blood grouping reagent used. Weak D (D\text{u}) red cell appear to be poorly immunogenic. Some partial D (D variant) cells may be immunogenic, especially those with a strong expression of the residual D antigen, such as some D\text{IV} cells.

RhD grouping methods should be validated for sensitivity and procedures adopted to maximise the detection of weak D (D\text{u}) and partial D (D variant) red cell as RhD positive

3. Quality Control of RhD Grouping

Quality control procedures recommended by reagents and equipment manufacturers should be followed.

Before a blood grouping reagent is used, appropriate reactivity with control red cell samples should be confirmed. (See Section 3.4.6.1). As a minimum, for each series of RhD blood grouping tests, unequivocal appropriate reactions must be obtained with Rir I red cells as a positive control and with r'r or rr red cells, as a negative control.

Appropriate reactivity with control red cell samples expressing weak D should also be confirmed regularly during use, although not necessarily with each series of tests.
2.2 Testing of Blood Donations (Optional, wherever feasible)

2.2.1 Additional Rh and K phenotyping

i) In the testing of donors being grouped for the first time, it is desirable that at least two anti-D blood grouping reagents should be used capable of detecting between them D\textsuperscript{W}, D\textsuperscript{V} and D\textsuperscript{w} antigens.

ii) Donors whose blood gives an unequivocal positive reaction with both anti-D reagents should be regarded as i.e. RhD positive.

iii) Donors whose blood is unequivocally negative with both anti-D reagents should be regarded as RhD negative.

iv) If the results with the anti-D reagents are discordant or equivocal, the tests should be repeated with another anti-D. Where the RhD group is in doubt it is safer to classify such donors as RhD positive.

v) For known (repeat) donors one anti-D reagent, or blended reagent that detects weak D, D\textsuperscript{W}, D\textsuperscript{V} and D\textsuperscript{w} can be used.

For some patients, e.g. those who have made anti-CD it may be necessary to provide blood negative for C, D and E antigens. This is achieved by testing RhD negative blood with blood grouping reagents containing anti-C and anti* E reactivity and applying an approved overstick label, e.g. CDE negative' to components from those donors who lack the C,D and E antigens.

Increasingly, blood is required that has been further Rh and/or K typed. For each series of these tests unequivocal, appropriate reactions must be obtained with, as a minimum, the following control cell samples:

<table>
<thead>
<tr>
<th>Blood grouping reagent</th>
<th>Control red cell samples</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td>Anti-C</td>
<td>R\textsubscript{1}r</td>
</tr>
<tr>
<td>Anti-E</td>
<td>R\textsubscript{2}r or r\textsuperscript{w}r</td>
</tr>
<tr>
<td>Anti-c</td>
<td>R\textsubscript{1}r or r\textsuperscript{w}r</td>
</tr>
<tr>
<td>Anti-e</td>
<td>R\textsubscript{2}r or r\textsuperscript{w}r</td>
</tr>
<tr>
<td>Anti-K</td>
<td>K+k+</td>
</tr>
</tbody>
</table>

Reagents used should comply with Section 2 of these Guidelines.

Before a new batch of blood grouping reagent is used, appropriate reactivity with control red cell samples should be confirmed.

2.2.2 Donation with a Positive Direct Antiglobulin Test
1. Red cell components and platelets from donations with a positive Direct Antiglobulin Test should not be used clinically.

2. Plasma from donations with a positive Direct Antiglobulin Test may be sent for fractionation, subject to the fractionator's specifications for 'starting material' being attained.

3. Donors whose Direct Antiglobulin Test remains positive for more than 1 year should be removed from the donor register and referred to the physician.

2.2.3 Donations found with allo-antibody

1. All donations should be tested for the presence of red cell antibodies of probable clinical significance by testing the donor's serum or plasma using a validated technique capable of detecting, unequivocally, anti-D at 0.5 IU/ml or lower (or at equal titration for 0.5 IU/ml).

The reagent red cell samples to be used for antibody screening should comply with Section 2 of these Guidelines.

2. Donations found to contain antibodies on routine screening should be further investigated, using an indirect antiglobulin technique and the specificity of any antibody determined.

3. If antibody is detected, samples of the serum or plasma diluted 1 in 10 and 1 in 50 should be tested by an indirect antiglobulin test using appropriate homozygous red cell samples; for anti-K Kk red cell samples may be used.

If anti-D is present, the level may be determined by serial dilution method or automated quantitation and expressed as IU/ml.

4. Blood and blood products with antibodies of probable clinical significance may be released, other than for neonatal use, as shown in the following table. Donations with high titre antibodies may be suitable resource for blood grouping reagents.
<table>
<thead>
<tr>
<th>Product</th>
<th>Potency of antibody of probable clinical significance</th>
<th>Fate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Anti-D IU/ml</strong></td>
<td><strong>Antibody</strong> in samples detected Diluted</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 in 10</td>
</tr>
<tr>
<td>Whole blood</td>
<td>4 IU/ml or greater</td>
<td>Detected</td>
</tr>
<tr>
<td></td>
<td>Less than 4 IU/ml</td>
<td>Detected</td>
</tr>
<tr>
<td>Red cells in SAG-M</td>
<td>10 IU/ml or greater</td>
<td>Detected</td>
</tr>
<tr>
<td></td>
<td>Less than 10 IU/ml</td>
<td>Detected</td>
</tr>
<tr>
<td>Cryoprecipitate</td>
<td>1 IU/ml or greater</td>
<td>Detected</td>
</tr>
<tr>
<td></td>
<td>Less than 1 IU/ml</td>
<td>Not Detected</td>
</tr>
<tr>
<td>Fresh Frozen Plasma</td>
<td>1 IU/ml or greater</td>
<td>Detected</td>
</tr>
<tr>
<td></td>
<td>Less than 1 IU/ml</td>
<td>Not Detected</td>
</tr>
<tr>
<td>Platelets</td>
<td>1 IU/ml or greater</td>
<td>Detected</td>
</tr>
<tr>
<td></td>
<td>Less than 1 IU/ml</td>
<td>Not Detected</td>
</tr>
<tr>
<td>Plasma for fractionation</td>
<td>10 IU/ml or greater</td>
<td>Detected</td>
</tr>
<tr>
<td></td>
<td>Less than 10 IU/ml</td>
<td>Detected</td>
</tr>
</tbody>
</table>

Notes: * If quantitated
** Including anti-D if not quantitated

2.2.4 Blood and blood products from group O donors with high-titres of anti-A, B

1. Plasma of a volume of 250 ml or more from a single donor may be infused into a patient who receives Fresh Frozen Plasma, platelets collected by apheresis, or platelets from several donations pooled in plasma from one
donation. This can result in haemolytic transfusion reactions in non-group O patients given such Fresh Frozen Plasma or platelets from group O donors.

Reactions are more likely to occur when components from group O donors with high titres of anti-A, B (titre of 128 or greater) are transfused into non-group O patients. Such group O donors are generally termed 'high-titre group O donors'. However, components from group O donors with lower titres of anti A-B also can cause intravascular haemolysis in non-group O recipients, of given in large enough volumes.

2. The serum or plasma of group O donors should be diluted 1 in 128 and tested with A and B red cell samples. Where there is an unequivocal positive reaction with either or both red cell sample, the following components for clinical use from such high-titre group O donors should be labelled 'for group 0 recipients only':

- Whole blood;
- Fresh Frozen Plasma (in volumes of 250ml or greater);
- apheresis platelet donations; and
- Pooled platelets containing plasma from a single high-titre group O donor

2.3 Screening for Transfusion Transmittable Diseases (TTDs)

2.3.1 In addition to blood group serology requirements, blood and blood components must not be released to stock unless they have been tested and found negative for HBsAg, anti-HIV 1 and 2, anti-HCV, antibodies to syphilis and also negative for malarial parasite. These tests have to be considered as mandatory.

2.3.2 Only assays deemed suitable by National Authorities in respect of sensitivity and specificity must be used for the detection of markers identified above. Additionally, testing sites must ensure that the expected standard of performance of assays is being achieved, by using appropriate assay batch pre-acceptance testing and statistical monitoring of test results on defined quality control samples.

2.3.3 The presence or absence of the microbiology markers described at 2.2.1 above should be determined by testing the serum of the donor. If plasma is used for testing, it must be handled according to the instructions accompanying the test kit. If there is a deviation from kit manufacturer's instructions, the variation must be validated to ensure it meets the required specificity and sensitivity criteria.

2.3.4 Initial Screen Reactive Samples

1. All initially reactive samples must be retested in duplicate, using the same assay as that used in the original test. This is an extremely important area of work and requires particular attention to ensure:

(i) that the correct sample is retrieved for repeat testing
(ii) that the actual sampling procedure for repeat testing is undertaken with due care,
(iii) that the results are carefully verified
(iv) that the overall integrity of the information transfer system is maintained.

2. If both the repeat screening tests are clearly non-reactive, the blood and any derived components can be released to stock.

3. If one or both of the repeat screening tests are reactive, the blood and any derived components must be labelled NOT FOR TRANSFUSION and a sample of plasma from the bleedline must be tested. The guidance given at 2.2.4 (i-iv) applies.

4. If the plasma sample from the bleedline produces the only clear negative result an investigation must be initiated according to local standard procedures to explain the apparent discrepancy.

5. If the donor is considered to be reactive for any of the mandatory microbiology tests described at 2.2.1, samples from the donor/ donation must undergo confirmatory testing at a designated reference laboratory.

i) If a positive result is confirmed, the donor record must be flagged as "permanent exclusion" risk- not to be bled for clinical use" or equivalent. Arrangements should be made to counsel and take repeat samples from the donor to confirm infection in the donor.

ii) If a negative or indeterminate result is reported following confirmatory testing, the procedure for reinstatement of such donors to active status is covered in section 2.2.6

2.3.5 Algorithm for Transfusion Transmittable Diseases (TTDs)
Initial screening test (serum)

Positive Reaction (place blood and all derived components)

Repeat Screening (serum x 2)

Any Repeat Test Positive
(label blood and all derived components - Not For Transfusion flag donor record)

Screening Test on Plasma from

Send Samples to a Reference Laboratory

Positive Result

Flag donor record as permanent deferral not to be bled for clinical use. Arrange counselling and investigation of donor

Blood group serology tests satisfactory

O Release to stock

Both Repeat Tests clearly non-reactive

Negative or Indeterminate Result for future action concerning the use of the donation risk and/or reinstatement of the donor to active status, see Chapter 1.

2.3.6 Reinstatement of donors whose serum has been confirmed to be falsely reactive in TTDs tests.

1. The procedures to be followed are described below and shown in the accompanying algorithm

   (i) Where an initial sample taken at donation in the Transfusion Centre is found repeatedly reactive (RR), materials from that donation must not be used for transfusion, and the donor's record must be flagged in accordance with standard operating, procedures and the donor removed from the active panel. No further material from the donor
must be used for clinical purpose until the donor has been returned to the active panel.
(ii) A specimen of the repeatedly reactive (RR) sample must be sent for confirmatory testing at a designated referral laboratory. If the specimen is considered to have been falsely reactive, reinstatement may be considered after a period of follow-up. The donor should be considered for reinstatement after at least six months,

(iii) A further specimen, taken at least six months after the initial bleed, must be sent to a designated reference laboratory. A number of options exist for re-instatement of the active panel depending upon the results of testing the six month follow-up sample at the Transfusion Centre and the designated reference laboratory. These are:

a) Sample now non-reactive in the current screening assay at the Transfusion Centre and confirmed negative at the designated reference laboratory. Action-return to active panel as eligible for future donations. The next donation may be used if a negative result is given on the current screening test.

b) Sample now non-reactive in the current screening assay at the transfusion Centre, discordantly reactive but considered falsely so at the designated reference laboratory. Action- return to active panel as eligible for future donations. The next donation may be used if a negative result is obtained in the current screening test.

c) Sample still reactive in the current screening assay used at the Transfusion Centre but non-reactive in an alternative assay at Transfusion Centre and either non-reactive or discordantly reactive but considered falsely so at the designated reference laboratory. Action-return to active panel as eligible for future donations if negative on an alternative screening test and the next donation used see section 2.2.6.2 below

2. In order to reinstate a donor whose serum remains falsely reactive in the original screening test the Transfusion Centre must refer this sample to the designated reference, centre which should run a different assay for flagged donors whose sera previously have been shown to give a false reaction in one particular assay. The following conditions must be met for this to be acceptable:

(i) At least six months must elapse between the date of the first RR sample and the follow up sample tested in the alternative assay.

(ii) The alternative assay must be of equivalent sensitivity to the first assay in which the original serum gave a repeatable reaction and conform to requirements of section 2.2.2.

(iii) The designated reference laboratory must have confirmed the false nature of the serum reactivity on a sample taken at least six months after the index donation.
(iv) Where archival samples are held on a donor, the RTC may adopt the strategy of testing samples taken at least six months, but not exceeding 12 months apart in the alternative assay in order to fulfill the criteria retrospectively.

(v) Donations taken subsequent to return to the active panel may be used provided that the donation is non-reactive by the alternative assay. The donor's record must remain flagged with the information identifying previous false reactivity for the marker.
ACTION CHART - DONOR REINSTATEMENT

Repeatedly Reactive at RTC
Indeterminate or Negative at Reference Laboratory

- Re bleed Donor (≥6 months after index donation)
  - RTC Routine Screen Procedure
    - Negative
      - Reference Laboratory
        - Indeterminate
          - Positive
            - Routine Screen with Alternative Validated Assay
              - Negative
                - Reference Laboratory
                  - Indeterminate
              - Positive
                - Reference Laboratory
                  - Positive

- Positive
  - Routine Screen with Alternative Validated Assay
    - Negative
      - Reference Laboratory
        - Positive
    - Positive
      - Reference Laboratory
        - Positive

Donation no to be used donor can be returned to active panel and next donation can be used if:
Sample negative at screening: Sample Negative with alternative assay

If donor present <6 months donation not be used and negative results at RTC and Ref. Lab. Disregarded for Reinstatement purposes
Notes:
1. Flag Donor Record (Recorded as permanent defer risk not to be bled for clinical use. Arrange counseling and investigation of donor).
2. Index donation for future reinstatement

2.3.7 Specific assays

1. HBsAg

   (i) Specification

   a) At present, public sector transfusion centres are being provided with HBV kits based mainly on haemagglutination or latex agglutination methods etc. Standard methodology and instructions (including for storage) by the manufacturer should be strictly observed using these commercially available assays.

   b) The recommended national specification for the minimum level of sensitivity for the performance of HBsAg screening using ELISA method has not yet been defined. A working standard should be available and must however give a positive reaction in each series of HIV 1 & 2 screening tests for the results of those tests to be valid.

   (ii) Quality Control of HBsAg Screening

   a) Each batch of HBsAg test kits should be shown to conform with locally established minimum criteria for specificity and sensitivity.

   b) In addition to the test kit manufacture's controls quality control measures should be taken with each series of tests to demonstrate acceptable sensitivity of the test method.

   c) No series of tests should be considered acceptable unless the result of the test kit manufacturer's and the additional quality control samples have satisfied the criteria laid down.

2. Anti-HIV1 and 2

   (i) Specification

   (a) At present, public sector transfusion centres are being provided with HIV kits based mainly on particle agglutination principle. Standard methodology and instructions (including for storage) by the manufacturer should be strictly observed using these commercially available assays.

   (b) The recommended national specification for the minimum level of sensitivity for the performance of anti-HIV 1 and 2 using ELISA method has not yet been defined. A working standard should be available and must however give a positive reaction in each series of HBsAg screening tests for the results of those tests to be valid.
(ii) Quality Control of Anti-HIV 1 and 2 Screening

(a) Each batch of anti-HIV 1 and 2 test kits should be shown to conform with locally established minimum criteria for specificity and sensitivity.

(b) In addition to the test kit manufacturer's controls, quality control measures should be taken to demonstrate acceptable sensitivity of the test method.

(c) No series of tests should be considered acceptable unless the result of the test kit manufacturer's and the additional quality control samples have satisfied the criteria laid down.

3. Anti-HCV

(i) Specification (ELISA)

The recommended specification for the minimum level of sensitivity for the performance of anti-HCV screening has not been defined. A working standard should be available and must however give a positive reaction in each series of HCV screening tests for the results of those tests to be valid.

(ii) Quality Control of Anti-HCV Screening

(a) Each batch of anti-HCV test kits should be shown to conform with locally established minimum criteria for specificity and sensitivity.

(b) In addition to the test kit manufacturer's control measures should be taken to demonstrate acceptable sensitivity of the test method.

(c) No series of tests should be considered acceptable unless the result of the test kit manufacturer's and the additional quality control samples have satisfied the criteria laid down.

4. Syphilis Antibody

(i) Specification

The specification for the minimum level of sensitivity, for the performance of syphilis antibody screening has not yet been defined beyond the requirement in each series of tests that a positive result must be obtained with the working standard.

(ii) Quality Control of Syphilis Anti-body Screening

a) Each batch of syphilis antibody test kits should be shown to conform with locally established minimum criteria for specificity and sensitivity.
b) In addition to the test kit manufacturer's quality control measures should be taken to demonstrate acceptable sensitivity of the test method.

c) No series of tests should be considered acceptable unless the result of the test kit manufacture's and the additional quality control samples have satisfied the criteria laid down,

4. Malarial Parasite

(i) Specification

Standard stains should be used to demonstrate the presence of malarial parasite.

(ii) Quality Control

(a) for respective staining method used should be observed as recommended for that particular procedure.

(b) Quality control measures should be taken to demonstration the acceptability of test method.

3. Additional Testing of Selected Donations

3.1 Antibody to Cytomegalovirus (anti-CMV)

3.1.1 The presence or absence of anti-CMV should be determined by examination of the serum or plasma of the donor. The recommended specification for the minimum level of sensitivity for the performance of anti-CMV screening has not yet been defined. A working standard should be available and must however give a positive reaction in each series of CMV screening tests for the results of those tests to be valid.

3.1.2 Although it is advisable to have panels of CMV seronegative donors, a donation must be considered anti-CMV negative and be labelled as such unless it has been tested and found to be anti-CMV negative.

3.1.3 Quality Control of Anti-CMV Tests

- Each batch of anti-CMV test kits should be shown to conform with locally established minimum criteria for specificity and sensitivity.

- In addition to the test kit manufacturer's controls quality control measures should be taken to demonstrate acceptable sensitivity of the test method.

- No series of tests should be considered acceptable unless the result of the test manufacturer's and the additional quality control samples have satisfied the criteria laid down.
Annex 4

Requirements for Safe and Effective Transportation of Blood and Blood Components

1. Transportation between donor sessions and blood centre

Blood and blood components collected at donor sessions must be transported to the receiving blood centre in appropriate conditions of temperature, security and hygiene, in accordance with a validated and documented procedure. Where it is intended to prepare platelet concentrates from the donation, the temperature (air) should not be allowed to drop below +18°C; otherwise, the minimum acceptable temperature is +2°C.

2. Whole blood and red cell components

Whole blood and red cell components issued by a blood centre must be transported to the receiving institution at a temperature (air) between +2°C and 10°C, in a containment system that assures adequate security and hygiene, in accordance with a validated and documented procedure.

3. Platelet

Platelet preparations issued by a blood centre must be transported to the receiving institution at a temperature (air) between +20°C and +24°C, in a containment system that assures adequate security and hygiene, in accordance with a validated and documented procedure.

4. Plasma components

Plasma components issued by a blood centre must be transported to the receiving institution in a containment system that assures adequate security and hygiene, in accordance with a validated and documented procedure designed to maintain the core storage temperature of -30°C during transportation.

5. Transfer between centres or hospitals

Blood and blood components that are to be transferred between blood centres or from one hospital blood bank to another should be transported under conditions equivalent to those defined in 2, 3 or 4 which ever is appropriate.

6. Containers

Standardized containers should be used to transport blood and blood products and these should bear a seal of BTS, Pakistan or relevant Blood Transfusion Authority.
Annex 5

Requirements for Blood Bag Labels

1. All blood groups should be represented by different and standard colour codes.
2. The contents of label should include:

   i. Component Produced at (name of the centre)
   ii. The Name of the Component: (name of the component)
   iii. The Volume of Component: _____________________
   iv. Donation Number: _____________________
   v. ABO Group: _____________________
   vi. RhD Group: _____________________
   vii. Date of Collection: _____________________
   viii. Temperature of Storage: _____________________
   ix. Date of issue: _____________________
   x. Slip issued with the blood bag should bear the remarks

Caution
"Component should not be used if there is any sign of determination"
SECTION 2

- General Guidelines for Serological Tests
- Serological Guidelines for ABO and RhD Blood Grouping Reagents.
- Guidelines for reagent Red Cells.
Chapter 1

General Guidelines for Serological Tests

1.1 Introduction

General guidelines applicable to all serological tests are presented in this chapter. In other chapters, additional guidelines are given for application in particular test systems.

Where the manufacturer provides a test system, the manufacturer's instruction should be followed.

1.2 Grading system for agglutination tests for manual tube tests.

The following grading system is used throughout these Guidelines for manual tube serological testing. If a cumulative (titration) score is required to assess the characteristics of a blood grouping reagent in a titration, then the score as indicated should be used.

<table>
<thead>
<tr>
<th>Reaction Grade</th>
<th>Description</th>
<th>Titration Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 5</td>
<td>Cell button remains in one clump or dislodges into a few large clumps, macroscopically visible.</td>
<td>12</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Cell button dislodges into numerous large clumps, macroscopically visible.</td>
<td>10</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Cell button dislodges into many small clumps, macroscopically visible.</td>
<td>8</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Cell button dislodges into finely granular but definite, small clumps, macroscopically visible.</td>
<td>5</td>
</tr>
<tr>
<td>Grade 1</td>
<td>Cell button dislodges into fine granules, microscopically visible.</td>
<td>3</td>
</tr>
<tr>
<td>Grade 0</td>
<td>&quot;Negative result&quot;</td>
<td>0</td>
</tr>
</tbody>
</table>

Unless otherwise stated, an unequivocal tube manual reaction is defined as a grade 3 or greater.

1.3 Test Red Cells.

1.3.1 Records should be kept of all red cells used in the assessment of a reagent during manufacture.

1.3.2 For specificity testing, red cells stored in the liquid state in a medium not specifically formulated to preserve the reactivity of antigens, should be used within 7 days of collection. Red cells stored in a medium proven to preserve the antigens for which the red cells are being used should be used within the shelf - life of red cells stored in that solution.

1.3.3 Red cells of any age may be used to test the potency and avidity of antibodies.
1.3.4 Red cells may be stored frozen and thawed for use in tests for potency, avidity and specificity. For use in tests for specificity the method of freezing, storage and thawing should be known to preserve the antigens for which testing will be performed. Frozen red cells should be used on the day they are thawed and resuspended unless they are suspended in a medium proven to preserve the antigens for which the red cells are being used, when they should be used within the validated shelf-life of red cells stored in that preservative medium.

1.3.5 Red cells for testing reagents for blood group serology that require an anti-human globulin technique, should give a negative test by a direct anti-human globulin test or with a reagent control tested by an indirect anti-human globulin technique.

1.3.6 Unless red cells are recommended for use without washing, red cells should be washed at least twice in saline before use. The supernatant after the last wash should be clear. Red cells to be suspended in LISS should be given at least one additional wash in LISS. Red cells suspended in saline or LISS should be discarded after 24 hours.

1.3.7 Red blood cells from different individuals used for specificity or potency tests should not be pooled except where otherwise stated in the characterization of antiglobulin reagents. Cord red cells of a given ABO and RhD group may be pooled.

1.3.8 Unless otherwise stated, the concentration of test red cell suspensions should be 2.3% by volume for normal ionic strength tests and 1.5-2% for low ionic strength tests.

1.3.9 Throughout this Section of the Guidelines, reference is made to the anti-coagulant CPD-A1. However, any anti-coagulant, licensed for the collection of blood for therapeutic use, may be used, if appropriate.

1.4 Test tubes

For manual tube tests, unless otherwise stated 10-12mm (diameter) x 75mm glass tubes should be used.

1.5 Centrifugation following the addition of anti-human globulin (AHG) reagent.

In the anti-human globulin technique, after the addition of the anti-human globulin reagent, the reactants should be centrifuged within 15-30 seconds of mixing, unless otherwise stated.

1.6 Centrifugation and reading serological tests.

1.6.1 Centrifugation.

The centrifugal force should be just sufficient to create a button of cells with clearly defined edges but not such to make the button difficult to dislodge. Many combinations of relative centrifugal force (rcf) and time may give similar results e.g. 110 rcf for 1 minute, 200 rcf for 30 seconds, 500 rcf for 15 seconds or 1000 rcf for 10 seconds.

1.6.2 Reading of tube tests.
1. Haemolysis

Haemolysis should be determined by the visual detection of haemoglobin in the supernatant fluid.

2. Agglutination.

A 'Shake' reading technique should not be used. Its over-vigorous action disrupts agglutination and is responsible for false negative tests in blood group serology.

Any of the following reading techniques may be used:

(i) Pipette transfer of cell button to microscope slides. The tube is not agitated at any stage. The transfer pipette is clean and has a 1.5-2.0 mm internal diameter bore and the tip is free from any irregularities. The cell button is drawn, by the minimum suction possible, into the stem of the clean pipette, then gently ejected onto a slide and simultaneously drawn out over an area of some 2cm$^2$. The angle of the pipette above the horizontal controls the width of the spread. The test is observed macroscopically, and microscopically if required."

(ii) Tip and roll. The tube is held almost horizontally (70-80° to the vertical) between the thumb and the first two fingers and slowly rotated without any shaking or agitation, until the cell button is dislodged from the tube. The free cell button /agglutinates are only allowed to move a maximum of 1cm down the tube. The test is read macroscopically, with the tube held horizontally over an illuminated light source. A x5 or x6 magnifying mirror, or a x6 hand lens can be used. Reading can then be obtained by examination of the tube placed horizontally on the stage of an inverted microscope.

(iii) Gentle agitation. The tube is held almost vertically between the thumb and first two fingers and gently agitated using a trembling or vibrating movement. The test is read as described above.

1.6.3 Reading of slide tests

The reagents are mixed thoroughly by rocking the slide for approximately 30 seconds with occasional further mixing during the incubation period. The test is observed macroscopically, and if required microscopically, for agglutination. This may be facilitated by reading over diffuse light resource.

1.6.4 Reading of microplate tests.

1. Resuspension technique in U-well microplates.

After incubation, the microplate should be centrifuged at 100 rcf or 40 seconds and the red cells gently dislodged using a shaker. The time required to achieve this will depend on the speed and orbit of the mixer. This has to be defined by observing known controls and turning off the shaker when cells in a known negative test should be fully resuspended and cells in a known weak-positive
test should remain clumped but dislodged. Over-agitation will reduce the strength of reaction or result in false-negative test results; under mixing will make reading difficult.

2. Streaming technique in V-well microplates.

After the final centrifugation step, the time and speed of which has to be determined for each technique, place the microplate at 70° to the horizontal, this is best done on a purpose built rack. The negative reactions will stream (trail) along with lower edge of the "V" part of the well, whereas a positive reaction will remain as a button of cells in the apex of the "V". The time taken to distinguish between weak positive and negative reactions depends on several variables, e.g. cell concentration, serum viscosity, force/ time of centrifugation. Known weak-positive and negative tests act as controls.

1.7 Non-serological tests

1.7.1 Manufacturers should ensure the correct concentration of those components of the formulation that may affect the performance of the reagent in blood group serology, for example, EDTA concentration, NaCl concentration, pH and total protein content.

1.8 Specificity tests.

1.8.1 The manufacturer should test the blood grouping reagent as a final product, by all methods recommended by the manufacturer for the specificity and reactivity claimed.

1.8.2 Specificity should be determined by testing the reagent with red cells from a minimum of 4 different donors known to express the antigen corresponding to the specificity of the reagent and 4 different individuals known to lack that antigen. The reagent should be tested for specificity by all methods recommended for its use by the manufacturer.

If a range of incubation times or incubation temperatures is recommended by the manufacturer, the range(s) should be used in these test procedures.

1.8.3 Contaminating antibodies to antigens having a prevalence of greater than 99 percent in the general population should be excluded by negative results in tests using samples of red cells from four different individuals who lack the antigen corresponding to the antibody specificity under test.

If tests using all methods recommended for use by the manufacturer do not exclude the presence of antibodies to the following antigens, these antibody specificities should be stated in the package insert as not having been excluded in specificity testing.

Xg\textsuperscript{a}, Do\textsuperscript{a}, Yr\textsuperscript{a}, Co\textsuperscript{b}, Wt\textsuperscript{a}, Bg\textsuperscript{a} and V\textsuperscript{w}

Where practicable, red cells for such testing should have homozygous expression of these antigens.
Subsequent batches, to the same formulation, of stable, well characterized monoclonal reagents need not be tested for contaminating antibodies to low frequency antigens.

1.8.4 Tests for the presence of contaminating ABO antibodies should be performed with red cells from a minimum of 2 individuals of group A1 and 2 group B who lack the antigen corresponding to the antibody specificity under test.

1.8.5 A blood grouping reagent recommended for use by a direct agglutination method should be tested against red cells lacking the antigen corresponding to the antibody specificity but coated with IgG blood group antibody to effect a grade 5 reaction in the anti-human globulin technique. Polyclonal IgG blood group antibodies from at least four individuals should be tested separately.

1.8.6 Blood grouping reagents which are chemically modified, and/or contain in their formulation a potentiator of agglutination, or require the user to add a potentiator, shall be tested, by all methods recommended by the manufacturer with red cells lacking the antigen corresponding to the antibody specificity under test but sensitized with an IgG Rh antibody to effect a grade 5 reaction in the anti-human globulin technique.

1.8.7 Requirements.

1. Blood grouping reagents should not produce a positive reaction when tested with red cells lacking the antigen corresponding to the antibody specificity under test, by any method recommended for use by the manufacturer. Should reactivity to a low frequency antigen be observed with subsequent batches of a reagent, this fact should be brought to the attention of all primary consignees of that reagent.

2. Blood grouping reagents recommended for use by a direct agglutination method should not contain antibodies reactive against red cells coated with IgG when used by direct agglutination methods recommended by the manufacturer.

3. A blood grouping reagent producing agglutination by those method recommended by the manufacturer should be supplied with a reagent control that has been shown to effect a degree of non-specific reaction with IgG coated red cells similar to the corresponding blood grouping reagent.

4. Rouleaux formation, prozone or haemolysis should not occur in tests using any of the methods recommended by the manufacturer.
Chapter 2

Serological Guidelines for ABO and RhD Blood Grouping Reagents

2.1 Introduction

2.1.1 The determination of the ABO and RhD group is of prime importance in ensuring the safe transfusion of blood. It is essential that reagents for ABO and RhD grouping are prepared using reliable manufacturing procedures that are consistently capable of producing safe and efficacious products.

2.1.2 The term weak D (D\(\text{w}\)) is used in these Guidelines to indicate a weakened expression of a normal D antigen. There is a gradation of the expression of the D antigen. Some high avidity IgM monoclonal anti-D will detect weak D in saline tests. However, in general, weak D (D\(\text{w}\)) cells are negative or weakly positive with IgM blood grouping reagents but are positive with IgG RhD blood grouping reagents used in an anti-human globulin technique.

2.1.3 The term D variant is used in these recommendations to indicate the expression of only a part of the normal D antigen. The reactivity of RhD blood grouping reagents against D variant red cells is determined by the nature of the D variant, the anti-D reagent and the technique used.

2.1.4 RhD grouping of donors: The reactivity of particular D variant cells in blood grouping procedures depends on the methodology and blood grouping reagent used. Although knowledge of D variants is still developing, low-grade weak D (D\(\text{w}\)) red cells appear to be poorly immunogenic. Some D variant cells may be immunogenic, especially those with a strong expression of the residual D, such as some D\(\text{v}\) cells.

RhD grouping procedures should be validated for sensitivity and procedures adopted to maximise the detection of weak D (D\(\text{w}\)) and D variant red cells as RhD positive.

In the testing of donors being grouped for the first time at a given Blood centre, at least two anti-D blood grouping reagents should be used; one detecting D\(^{+}\) red cells, the other not. This should enable D\(^{\text{VI}}\) female donors of child-bearing age to be identified in order to avoid their exposure to RhD positive blood: D\(^{+}\) individuals may develop "anti-D" to those epitopes absent from their D antigens, in response to pregnancy or transfusion.

2.1.5 RhD grouping of patients: anti-D blood grouping reagents for RhD grouping of patients should not react with D\(^{+}\) red cells using the method(s) recommended for use. "Follow-on" tests of negative results using an antiglobulin procedure are not recommended.

2.2 Specificity of ABO blood grouping reagents

2.2.1 Method
1. With due regard to the requirements of 2.9, as a minimum the following red cells should be tested using all methods recommended for use by the manufacturer.

<table>
<thead>
<tr>
<th>Blood Grouping Reagent</th>
<th>Minimum number of red cell samples to be tested</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A1</td>
</tr>
<tr>
<td>Anti-A</td>
<td>2</td>
</tr>
<tr>
<td>Anti-B</td>
<td>2</td>
</tr>
<tr>
<td>Anti-A,B</td>
<td>1</td>
</tr>
<tr>
<td>Anti- A+B</td>
<td>1</td>
</tr>
</tbody>
</table>

* only if the anti-A is recommended for the detection of A_x cells.

1. If further reactivity is claimed by the manufacturer against subgroups of A other than A1, A2 and A_n, red cells from at least three individuals of each additionally claimed subgroup should be tested.

2. If further reactivity is claimed by the manufacturer against subgroups of B, red cells from at least three individuals of each additionally claimed subgroup together with red cells from at least three individuals of the subgroups B3 and Bv should be tested.

3. In addition, three group A, three group B and three group O individual cord red cell samples should be tested by the methods recommended for use by the manufacturer. Manufacturers should be aware that some populations particularly Chinese, have a weakened or partial expression of A and/or B antigens.

2.2.2 Requirements

1. The blood grouping reagent is satisfactory if an unequivocal positive result is obtained with all the red cell samples having the antigen corresponding to the blood group reagent being assessed, by all the methods recommended for use by the manufacturer.

2. In addition, anti-A blood grouping reagent is satisfactory if an unequivocal positive result is obtained with all the A2B samples tested by all the methods recommended for use by the manufacturer.

3. In addition, anti-A, B blood grouping reagents and anti-A blood grouping reagents recommended for the detection of A_x should effect an unequivocal positive result with each of the A_x red cell samples tested by those techniques recommended by the manufacturer for the detection of A_x.

4. In addition, blood grouping reagents which are claimed to detect subgroups of A other than A1; A2 and A_x should effect an unequivocal positive result with each of the red cell subgroup by those techniques recommended by the manufacturer for the detection of those subgroups.
5. In addition, blood grouping reagents which are claimed to detect subgroups of B, should effect an unequivocal positive result with each of the red cell subgroup samples by those techniques recommended by the manufacturer for the detection of those subgroups and with each of the B$_3$ and B$_v$ subgroup samples by these techniques.

6. In addition, blood grouping reagents should effect an appropriate unequivocal reaction with each of the cord red cells samples by all those techniques recommended for use by the manufacturer.

**Potency of ABO blood grouping reagents used in manual or microplate tests.**

2.3.1 Method

The blood grouping reagent should be tested by the methods recommended for use by the manufacturer with red cell samples as shown in the following table. It should be tested undiluted, that is as recommended for use, and diluted using a medium with a formulation identical to the blood grouping reagent but with antibody protein replaced by non-antibody protein, e.g. fetal calf serum or bovine serum albumin.

<table>
<thead>
<tr>
<th>Blood Grouping Reagent</th>
<th>Minimum number of red cell samples to be tested</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A$_1$</td>
</tr>
<tr>
<td>Anti-A</td>
<td>1</td>
</tr>
<tr>
<td>Anti-B</td>
<td></td>
</tr>
<tr>
<td>Anti-A,B</td>
<td>1</td>
</tr>
<tr>
<td>Anti- A+B</td>
<td>1</td>
</tr>
</tbody>
</table>

2. Requirements

1. anti-A blood grouping reagents should effect a potency titre at least equal to the reference anti-A preparation with the red cell samples tested.

2. anti-B blood grouping reagents should effect a potency titre at least equal to the reference anti-B preparation with the red cell samples tested.

3. anti A, B blood grouping reagents should effect a potency titre at least equal to the reference anti-A preparation with the A$_1$ and A$_2$ red cell samples tested and a potency titre at least equal to the reference anti-B preparation with the group B red cell samples tested.

4. anti-A+B blood grouping reagents should effect a potency titre at least equal to the reference anti-A preparation with the A$_1$ and A$_2$ red cell samples tested and a potency titre at least equal to the reference anti-B preparation with the group B red cell samples tested.

2.4 Avidity of ABO blood grouping reagents used in manual slide tests

2.4.1 Method

As a minimum, the following red cell samples should be used.
Standards and Guidelines for Stored Transfusion Services, Pakistan.

<table>
<thead>
<tr>
<th>Blood Grouping Reagent</th>
<th>Minimum number of red cell samples to be tested</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( A_1 )</td>
</tr>
<tr>
<td>Anti-A</td>
<td>1</td>
</tr>
<tr>
<td>Anti-B</td>
<td>1</td>
</tr>
<tr>
<td>Anti-A,B</td>
<td>1</td>
</tr>
<tr>
<td>Anti-A+B</td>
<td>1</td>
</tr>
</tbody>
</table>

2.4.2 Requirements

There should be an unequivocal positive result within one minute of mixing.

2.5 Specificity of anti-D blood grouping reagents used in manual or microplate tests.

2.5.1 Method

With due regard to the requirements of 2.9 as a minimum the following red cells should be tested using all methods recommended for use by the manufacturer:

- \( r_r \) from two individuals
- \( r_r \) or \( R_0 \) \( R_0 \) from two individuals
- \( r^j \) \( r^j \) from one individual
- \( r^j \) \( r^j \) from one individual
- \( r_r \) from one individual

Anti-D blood grouping reagents which include polyclonal material and are recommended by the manufacturer for use by the anti-human globulin technique should be tested with a minimum of three \( r_r \) cells with strong expression of Bg'.

Anti-D blood grouping reagents recommended by the manufacturer for the detection of weak D (Dw) should be tested with a minimum of three weak D (Dw) red cell samples using those techniques recommended by the manufacturer for the detection weak D (Dw).

Anti-D blood grouping reagents recommended by the manufacturer for the detection of D variant should be tested with a minimum of 2 examples of the particular D variant against which reactivity is claimed, using those techniques recommended by the manufacturer for the detection of that D variant.

2.5.2 Requirements

1. Anti-D blood grouping reagents should effect an unequivocal positive result with all D positive red cell samples by all methods recommended for use by the manufacturer and negative reactions with D negative red cell samples.

2. Anti-D blood grouping reagents, if recommended for use by the anti-human globulin technique should effect negative reactions with \( r_r \) cells with a strong expression of the Bg' antigen.

3. Anti-D blood grouping reagents recommended by the manufacturer for the detection of weak D (Dw) should effect an unequivocal positive result with the three weak D
(D<sup>v</sup>) red cell samples using those techniques recommended by the manufacturer for the detection of weak D (D<sup>v</sup>).

4. Anti-D blood grouping reagent recommended by the manufacturer for the detection of D variants should effect an unequivocal positive reaction with the 2 examples of the particular D variant against which reactivity is claimed, using those techniques recommended by the manufacturer for the detection of that D variant.

5. **RhD grouping of patients**: anti-D blood grouping reagents for RhD grouping of **patients** should not react with D<sup>VI</sup> red cells. In the testing of donors being grouped for the first time, at least one anti-D reagent capable of detecting D<sup>v</sup> red cells should be used.

### 2.6 Potency of anti-D blood reagents used in manual or microplate tests.

#### 2.6.1 Method

1. As a minimum, pooled red cells from four R<sub>1r</sub> individuals should be tested by the methods recommended for use.

2. For monoclonal IgM anti-D blood grouping reagents, the potency titre should be determined in parallel with the reference preparation for anti-D (IgM).

3. For other anti-D blood grouping reagents, the reagent is tested undiluted, that is-as recommended for use, and diluted using a diluent of a formulation identical to the reagent but with antibody protein replaced by non-antibody protein e.g. fetal calf serum or bovine serum albumin.

#### 2.6.2 Requirements

1. For monoclonal IgM blood grouping reagents. The potency titre should be at least that of the reference preparation.

2. For other anti-D blood grouping reagents. There should be an unequivocal positive result with the undiluted reagent and with the reagent diluted 1 in 8.

#### 2.6.3 Method

As a minimum, red cells from four R<sub>1r</sub> individuals should be tested by the methods recommended for use.

#### 2.6.4 Requirements

The kit component should effect an unequivocal positive result with all the R<sub>1r</sub> test red cell samples.

### 2.7 Avidity of anti-D grouping reagents used in manual slide tests

#### 2.7.1 Method

As a minimum, R<sub>1r</sub> red cells from 2 individuals should be used.

#### 2.7.2 Requirements

There should be an unequivocal positive result within one minute of mixing.
Chapter 3

Guidelines for Reagent Red Cells

3.1 Guidelines for testing reagent red cells.

1.1.1 When testing reagent red cells, in order to confirm the presence or absence of antigens listed in the antigen profile, a sample from each individual (especially from those not used previously for such reagent red cells) should be tested whenever possible, with a minimum of two different examples of blood grouping reagents corresponding to each antigen specifically listed.

1.1.2 Where such testing produces conflicting results, repeat and further testing with at least one additional example of the relevant antibody(ies) should be undertaken before the antigenic status of that cell is committed to the antigen profile included within the package insert.

1.1.3 Where such testing has been performed with only one example of any blood grouping reagent, this information should be stated in the antigen profile included within the package insert.

1.1.4 Reagent red cells should be shown not to produce unwanted positive reaction by the methods recommended for use by the manufacturer.

1.1.5 Except for IgG sensitized and C3-sensitised red cells should be negative in the direct anti-human globulin technique with anti-IgG, anti-complement and polyspecific anti-human globulin reagents using the techniques recommended for use by the reagent manufacturer.

3.2 Preparation of reagent red cells

3.2.1 Red cells for use in reverse ABO grouping, in the control of blood grouping reagents, or in the detection of irregular antibodies in blood donations, may be pooled by a procedure which ensures adequate mixing of the constituent red cells.

3.2.2 With the exception of umbilical cord blood, red cells used to test patient's samples for irregular antibodies should not be pooled.

3.2.3 Reagent red cells should be processed by a method consistently shown to yield a product capable of detecting, throughout its shelf life, all antibodies directed against the antigens specified in the antigen profile included within the package insert.

3.2.4 Unless instructions are given to wash the reagent red cells before use, all reagent red cells should be free of ABH specific blood group substances and blood group antibodies, including anti-A and anti-B, demonstrable by the manufacturer's recommended methods of use. If the reagent red cells are to be washed by the user, the package insert should give instructions on the washing procedure.
3.2.5 The method of manufacture should ensure that white cells are removed from
donations of red cells before the white cells lyse and release enzymes, which may
adversely affect the properties of the red cells.

3.3 **Enzyme treated reagent red cells.**

3.3.1 Reagent red cells pretreated with proteolytic enzymes may be provided for antibody
screening and identification.

3.3.2 The method of enzyme treated used by the manufacturer should be shown
consistently to yield a product capable of detecting, throughout its shelf-life, those
antibodies which the reagent is intended to detect and minimise unwanted positive
reactions.

3.4 **Reagent red cells for use in ABO grouping**

3.4.1 Reagent red cells for use in ABO grouping need only be grouped for A; A1; B and
RhD.

3.4.2 Reagent red cells for reverse grouping.

Reagent red cells should be groups A1 and B and should be RhD negative. In
addition, A2 RhD negative red cells may be included.

3.4.3 Controls for ABO blood grouping reagents.

Reagent red cells of groups A1; A2, B and O should be used for the control of each
batch of tests with anti-A; anti-B; anti AB, anti A+B or anti-A1.

3.5 **Reagent red cells for use in RhD grouping**

3.5.1 Reagent red cells for the control of RhD blood grouping need only be ABO grouped
and Rh phenotyped with anti-C; anti D; anti-E; anti e.

3.5.2 Controls for RhD blood grouping reagents.

For polyclonal RhD blood grouping reagents, reagent red cells of groups OR,r, Or1 r,
A1rr and Brr should be used for the control of each batch of RhD blood grouping
tests.

3.5.3 For monoclonal RhD blood grouping reagents, reagent red cells of groups OR,r, and rr,
which may be group O, A1 or B, should be used for the control of each batch of RhD
blood grouping tests.

3.6 **Reagent red cells for use in antibody screening**

3.6.1 Introduction

The detection of irregular antibodies in the serum of a patients of greater clinical
significance than if such antibodies are detected in blood donors. Consequently it is
permissible to use reagent red cells of a lesser specification when performing antibody screening tests on blood donor samples.

3.6.2 General

1. Reagent red cells for use in antibody screening should be confirmed as group 0 by an ABO blood grouping procedure which is capable of demonstrating the Ax phenotype.

2. Where practicable, regent red cells known to express low frequency antigens (that is, those antigens having a frequency of less than 1 percent in the general population of the UK) should not be included in reagent red cells for antibody screening.

3. Where practicable, red cells from individuals known consistently to effect troublesome reactions with HLA specific antibodies should not be used as reagent red cells for antibody screening.

3.6.3 Reagent red cells for use in antibody screening of patient samples

1. General guidelines

2. As a minimum the following antigens should be expressed on the regent red cells for antibody screening: C; c; D; E; e; K; k; Fy^a; Fy^b; Jk^a; Jk^b; S; s; M; N; p1; Le^a and Le^b.

3. As a minimum, reagent red cells from two individuals should be provided. These red cells should not be pooled.

4. At least one of the red cell samples should express the probable Rh.haplotype R_2.

5. Apparent homozygous expression of the following antigens is desirable; D; E; Fy^a; Fy^b; Jk^a; Jk^b; S and s.

3.6.4 Reagent red cells for use in antibody screening of donor samples

1. General guidelines

2. It is preferable that reagent red cells are provided, unpooled, from a minimum of two individuals but the reagent may be supplied as a pool of red cells from no more than two donors.

3. Pooled reagent red cells for antibody screening should be used only for testing samples from blood donors; not samples from patients.

4. As a minimum the following antigens should be expressed:
   D; C; c; E; e; K

5. At least one of the red cell samples should express the probable Rh.haplotype R_2.
3.7 Reagent red cells for use in antibody identification

3.7.1 General guidelines

1. Reagent cells for use in the identification of irregular antibodies should be confirmed as group by an ABO blood grouping procedure which is capable of demonstrating the Ax phenotype.

2. Where practicable, red cells from individuals known consistently to effect troublesome reactions with HLA specific antibodies should not be used in reagent red cells for antibody dentification.

3. Reagent red cells for antibody identification should comprise red cells from eight or more group O individuals and permit the confident identification of those clinically significant alloantibodies which are most frequently encountered, for example, anti-D, anti-E, anti-c, anti-K and anti-Fy^a.

4. Red cells from the eight or more individuals which comprise the red cell panel for antibody identification, should be tested, as a minimum, with antibodies of the following specificities; C; C^w; c; D; e; E; k; k; Kp^a; Fy^a; Fy^b; Jk^a; Jk^b; S; s; Le^a; Le^b; M; N; P, and Lu^a.

5. A distinct pattern of reactivity should be apparent for each of the commonly encountered alloantibodies, for example, anti-D, anti-E, anti-c, anti-K and anti-Fy^a.

6. The antigen profile of reagent red cells for antibody identification, as far as possible, should permit assignment of specificity in test sera containing more than one commonly encountered alloantibody, for example, anti-D+K.

7. For reagent red cells for antibody identification, the minimum characteristics are:

   (i) Red cells from one individual should be R^1R^1 and from another individual should be R^1W R^1. Between them, these two individuals should express the antigens: K; k; Fy^a; Fy^b; Jk^a; Jk^b; S and s.

   (ii) Red cells from one individual should be R^2 R^2, those from another individual should be r^r and those from another individual should be r^r.

   (iii) Red cells from a minimum of three individuals should lack the Rh antigens C, E and D. One of these three individuals should be K positive. Between them, red cells from these individuals should exhibit apparent homozygous expression of the antigens: c;k; Fy^a; Fy^b; Jk^a; Jk^b; S and s.

3.8 Reagent red cells for use in the control of the anti-human globulin technique

Anti-IgG activity in negative anti-human globulin tests.
1. In order to confirm that each anti-human globulin test has been conducted correctly, reagent red cells sensitised with IgG antibody should be added to all negative tests.

Strongly sensitised reagent red cells can be agglutinated by an anti-human globulin reagent that has been partially neutralised by residual human protein to an extent that weak antibodies are not detected. Whereas, in the same circumstances, weakly IgG sensitised reagent red cells are not agglutinated.

The agglutination of sensitised reagent red cells by the anti-human globulin reagent is weakened when the sensitised reagent red cells are mixed with well-washed test red cells with no bound IgG antibody in the presence of anti-human globulin reagent.

Reagent red cells for this purpose may be provided ready for use, comprising a suspension of reagent red cells sensitised with IgG antibody.

2. Test Method

Add one volume of 2-3% well-washed unsensitised group O red cells to two tubes.

Add two volumes of the anti-IgG reference preparation to each tube. Mix well, Centrifuge and observe for agglutination which should not be present.

Add one volume of a 1 in 1000 dilution of human serum in saline to one tube and one volume of saline to the other.

Add one volume of the sensitised reagent red cells. Mix, incubate at 19-25°C for one minute, centrifuge and observe for agglutination.

3. Requirement

The test with the 1 in 1000 dilution of serum should be negative or give a reaction grade of 1; the other test should have a grade 2-4 reaction.
SECTION 3

Guidelines for Clinical use of Blood and Blood Products

- Red Cell Preparations
- Platelet Concentrates
- Plasma
- Albumin
- Intra Venous (IV) Immune Globulin
- Haemophilia Treatment.
Chapter 1

Clinical use of Red Blood Cell Preparations

1. Blood Transfusion in Surgical Patients

1.1 Pre-operative and Per-Operative Patients

There is no indication to transfuse patients to achieve a post-operative haemoglobin greater than 10 g/dl. For example, where a patient's hemoglobin is not expected to fall below l0g/dl as a result of per-operative blood loss, blood transfusion will generally not be necessary; circulating blood volume should be maintained using infusion of crystalloid or colloids solution or a combination of crystalloid and colloid solutions. This is true, irrespective of the presence or absence of pre-existing coronary disease.

Current evidence suggests that a patient whose pre-operative hemoglobin is between 8 and 10 g/dl. can be expected to tolerate blood loss of up to 500 ml. without compromise, providing the circulation blood volume is maintained using crystalloid or colloid solutions, even in the presence of pre-existing coronary vessel disease. However, in patients worth clinical evidence of cardiac or respiratory disease, and in patients older than 45 years, or in the presence of continuing blood loss, blood transfusion to maintain the haemoglobin between 8-10 g/dl. should be considered.

Patients whose pre-operative haemoglobin is less than 8 g/dl. will be at increased risk if the blood loss is likely to exceed 500 mis. Younger, previously fit patients would be expected to tolerate lower haemoglobin or higher blood losses in most cases.

In large volume continuing blood losses, whole blood is an appropriate source of red blood cells, but red cell concentrate is also appropriate.

1.2 Blood Transfusion in Acute Hemorrhage from Trauma, Obstetric Hemorrhage, and Castro-Intestinal Hemorrhage.

It is far more important to maintain circulating blood volume than to restore red cell loss in the first instance, by using crystalloid or colloid solutions, or a combination of these. Therefore, resuscitation should be begun with infusion of suitably large volumes of crystalloid/colloid; blood transfusion should, if possible, be begun by the time the blood loss approaches 50% of the physiological blood volume. While stored blood within the first two weeks of its shelf-life may be preferable to older units, stored blood throughout its shelf-life is acceptable.

In large volume continuing blood losses, whole blood is an appropriate source of red blood cells, but red cell concentrate is also appropriate.

2. Blood Transfusion for Medical Patients.

In reversible anaemias, either acute or chronic, such as megaloblastic anemia, iron deficiency, acute malaria in young children, reversible hemolytic events and sickle crisis, blood
transfusion should not be given, unless the patient's life is in danger, for example in the presence of cardio-respiratory decompensation; specific therapy should be started instead.

In chronic irreversible anemia, for example thalassaemia major, sickle cell disease, chronic renal failure, blood transfusions may be required to improve the patient's symptoms or as part of a hyper transfusion programme. Red Cell concentrate is preferrable to whole blood in these patients.
Chapter 2

Guidelines for Clinical Use of Platelet Concentrates

Although platelet concentrates currently play a relatively minor role in transfusion medicine in Pakistan, it is likely that the growth of treatment for haematological malignancies and solid tumours will increase demand steeply in the future.

Platelet transfusions are indicated for the treatment and prevention of hemorrhage due to thrombocytopenia or platelet dysfunction. This may involve short-term treatment of an isolated incident, or repeated, prolonged platelet therapy.

It is essential that the cause of thrombocytopenia is diagnosed before instituting platelet therapy.

An adult dose of platelets usually contains at least $240 \times 10^9$ platelets which can be provided by pooling platelets from 4 to 6 blood donations, or by a single apheresis unit.

**Clinical indications for platelet transfusion:**

1. Bone marrow failure
   1.1. Self-limiting conditions due to cytotoxic drugs, radiotherapy, leukaemias and other malignancies prior to remission.
   1.2. Chronic failure due to aplastic anaemia or infiltration not undergoing definitive treatment.

   Significant spontaneous thrombocytopenic bleeding is not likely to occur at platelet counts above $10 \times 10^9/\ell$. Minor mucosal bleeding or purpura may occur at platelet counts under $50 \times 10^9/\ell$.

2. Prophylactic platelet transfusion

   The use of platelets for stable, afebrile patients to keep the platelet count above $10 \times 10^9/\ell$ reduces the risk of hemorrhage as effectively as keeping it above any higher level.

   In other cases, where fever, sepsis or concurrent coagulopathy exist, or when minor surgery is required, the following schedule of therapy should be considered:

<table>
<thead>
<tr>
<th>Morning Platelet Count ($10^9$)</th>
<th>Indications for Prophylactic Platelet Transfusions on the same day</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>In every Case</td>
</tr>
<tr>
<td>10 to 15</td>
<td>In the presence of:</td>
</tr>
<tr>
<td></td>
<td>• fresh minor haemorrhage</td>
</tr>
<tr>
<td></td>
<td>• body temp, over $38^\circ$</td>
</tr>
<tr>
<td>15 to 20</td>
<td>In the presence of:</td>
</tr>
<tr>
<td></td>
<td>• coagulation disorders and/ or heparin</td>
</tr>
<tr>
<td></td>
<td>• before bone marrow biopsy or lumbar puncture</td>
</tr>
</tbody>
</table>
Over 20

In the presence, and until control of major bleeding complications
• before minor surgical procedures (other biopsies, central venous catheter insertion, arterial punctures ...)

3. Immune Thrombocytopenia

3.1 Auto-immune Thrombocytopenia (ITP)

Platelet transfusions are not usually indicated in cases of ITP as other forms of therapy are more effective and safer. This is also true prior to splenectomy in ITP.

They may be useful in large doses, however, in the presence of major, life-threatening hemorrhage, or incipient cerebral bleeding.

3.2 Platelet transfusions are not effective in post transfusion purpura, where intravenous immune globulin is the treatment of choice.

3.3 Neonatal Allo-Immune Thrombocytopenia, causing severe thrombocytopenia can be treated with platelet concentrates prepared from maternal donations. However, maternal platelets must be washed (to remove platelet-specific antibody) and irradiated (to avoid transfusion graft vs host disease).

4. Massive Blood Transfusion

Clinically significant dilutional thrombocytopenia only occurs with transfusion over 1.5 times the total blood volume.

There is no evidence that prophylactic platelet or plasma administration to patients receiving large volume transfusion reduces the risk of Microvascular Bleeding (MVB)

5. Cardio-Pulmonary Bypass Surgery

Prophylactic platelet transfusions are not required for patients under going such procedures.

Platelet dysfunction and/or thrombocytopenia may occur as a result of bypass surgery (particularly when bubble-oxygenators are employed). Platelet transfusion may be required in such cases, when bleeding occurs.

6. Disseminated Intravascular Coagulation (DIC)

In acute DIC, when bleeding is associated with thrombocytopenia, platelet transfusion should be given as part of general replacement therapy.

It may be necessary to raise the circulating platelet count to between 50,000 and 100,000x10⁹/l. because of platelet dysfunction.
Chapter 3

Guidelines for Clinical Use of Plasma

Frozen Fresh Plasma is taken to indicate the plasma separated from a standard donation of blood (normal 450+10% ml.) within 8 hours of collection and stored at less than -30°C. Plasma collected and stored in this way can be kept for 18 months. Plasma stored at temperatures higher than -25°C may be unstable and will have a shorter shelf-life for the purposes of labile coagulated factors (Factor V and VIIIc).

Cryosupematant Plasma is plasma frozen after removal of cryoprecipitate. It will contain less than half of the normal plasma concentration of fibrinogen, and very diminished concentrations of VIIc, vWF and XIII. In other respects, it is similar.

FFP is used for the treatment of impaired haemostasis caused by multiple factor deficiencies. These include DIC, liver disease and dilution coagulopathy and massive transfusion (often associated with some degree of DIC).

1. **Disseminated Intravascular Coagulation (DIC):** Plasma can be used to correct coagulation deficiencies in patients who are bleeding or at risk of bleeding.

   In these patients, platelet transfusion may also be necessary to correct the haemostatic defect.

   Loss of fibrinogen, F.VIIIc and F.V can be disproportionately large in these patients and cryoprecipitate is often indicated.

   **Dose:** at least 3 to 6 units of FFP will be required in a normal sized adult.

2. **Dilution Coagulopathy:** Patients who have lost over one whole blood volume replaced with colloid and/or crystalloid and stored blood may develop a coagulopathy due, in the first place, to thrombocytopenia. More severe blood losses and replacement will result in critically low levels of coagulation factors. There is no place, however, for "formula" replacement of coagulation factors by FFP (eg one unit of FFP following each 4 to 6 units of stored blood) which has no benefit.

   - Patients who have had hypotensive episodes will tend to develop critical loss of platelets and coagulation factors more quickly due to DIC
   - Patients who have developed a coagulopathy in association with massive transfusion (with or without DIC and/or sepsis) will manifest as microvascular bleeding a diffuse oozing from wound surfaces.

   **Dose:** as above

3. **Liver Disease:** Patients with severe parenchymal liver disease may have reduced levels of clotting factors. Blood product therapy is not indicated simply to correct prolonged clotting times, but may be useful in the treatment of hemorrhage in these patients, or as prophylaxis for elective surgical procedures:
• Complete correction of clotting time is not usually possible with plasma, therapy alone. Indeed, the volumes of plasma required to exert a measurable effect may not be tolerated by these patients. Prothrombin complex concentrates (II, IX, X and if available with additional F.VII) can be used in association with plasma to correct the coagulopathy associated with liver disease. However, these concentrates are thrombogenic and may exacerbate the clinical condition, and are costly as well.

• Patients with pre-existing liver disease are especially at risk for transfusion-transmitted hepatitis.

• In thrombotic thrombocytopenic purpura (TTP), cryosupernatant plasma and FFP, with or without plasma exchange, are the treatment of choice, and are needed in large volumes (over 3 litres/day)

   Even though the use of stored or frozen fresh plasma and cryosupernatant plasma are usually prescribed in the management of hypovolaemia where safer crystalloids, synthetic colloid solutions, or 4.5% to 5% albumin are available, when they are not, qualified support may be given to their use in this setting.

• Where there is an active haemophilia care programme calling for significant cryoprecipitate production, the most cost-effective option is cryosupernatant plasma, rather than FFP.

• Nutritional Support and protein-losing conditions.

• There is no justification for using FFP for nutritional purposes, for chronic diarrhoea, cirrhosis or nephrosis, including protein-losing enteropathy.
Chapter 4

Guidelines for Clinical use of Albumin

1. Indications for Human Albumin Solutions:

   1.1. Albumin 4.5% to 5%
       • Volume Replacement for severe blood loss (over 30% of total blood volume).
       • Severe burns
       • Replacement solution in therapeutic plasma exchange (frequently diluted with crystalloids).
       • Septic shock with or without hypoproteinaemia.

   1.2. Albumin 18% to 20%
       • Before or following extensive surgery
       • In severe sepsis
       • In Adult Respiratory Distress Syndrome (ARDS)
       • In the initial management of acute cirrhosis and nephrosis

2. Conditions for which Albumin is not indicated.

   • Malnutrition or undernutrition
   • Chronic cirrhosis and nephrosis
   • Protein- losing enteropathy
   • Promotion of wound- healing
Chapter 5

Clinical Guidelines for Intravenous Immune Globulin (I.V.ig)

1. Treatment of First Choice:

1.1. Primary and secondary humoral immuno-deficiency
   (0.2-0.4 g/kg, 2-weekly)
   - Includes some cases of Chronic Lymphocytic
     Leukaemia and Myeloma in stable phase

1.2. Immuno-modulation of auto-immune disease:
   - Kawasaki's Vasculitis, with concurrent aspirin
     (1/g/kg. for 2 days, started within 10 days of onset)
   - Guillain-Barre polyneuritis (0.4 g/ kg. for 5 days)

1.3 Post-transfusion purpura (FTP)

2. Treatment of second choice

2.1. Immune-mediated thrombocytopenia (ITP)
   0.4 g/kg. for 5 days, although there is some evidence that smaller doses are
   beneficial).
   - Prednisolone is generally the treatment of first choice in severe
     thrombocytopenia
   - i.V. Ig. is most effective in children with acute ITP.
   - In adults, the effect may be transient and therapy is most effective when used to
     obtain a rapid platelet increase in preparation for surgery.

2.2. May be effective in preventing CMV-mediated pneumonitis and mitigating
     GvHD following allogeneic bone marrow transplantation

2.3. Valuable in acquired Factor VIII/IX deficiency due to inhibitor formation when
     bleeding occurs.

2.4 Unproven Benefit
   - Premature, underweight neonates, to prevent infection.
   - Burns, to prevent bacterial infection
   - Uncertain application in paediatric HIV infection
Chapter 6

Clinical Guidelines for Haemophilia Treatment

The cardinal principles for successful management of severe haemophilia to prevent irreversible, progressive changes due to repeated hemorrhages in muscles and joints, include:

- Initiating treatment early in life
- Administering an effective dose of specific replacement therapy
- Undertaking treatment of haemarthroses and haematomas as early as possible, preferably by instituting home therapy

1. Early appropriate replacement therapy for haemarthroses and haematomas or, better still, prophylactic coagulant factor treatment have been shown to be highly cost-effective. Patient outcomes, in the long term, are significantly improved, and overall coagulant factor utilisation is strikingly reduced.

2. In the light of the life-long dependence of these patients upon replacement therapy, every precaution must be taken to:
   - Conserve their veins
   - To maintain good muscular development through regular, mild, exercise or physiotherapy
   - Ensure that, if cryoprecipitate is utilised, it is derived from carefully selected blood donors who have been tested for evidence or transfusion transmitted infection
   - Immunise previously untransfused haemophiliacs against Hepatitis B virus, if possible.

Currently licensed industrial factor concentrates have all been virally inactivated. Major orthopaedic and soft-tissue surgery can safely be carried out with adequate availability of specific concentrates for replacement therapy, and reliable laboratory support.

3. Von Willebrand factor deficiencies should preferentially be treated with l-desamino-8-D arginine vasopression (DDAVP), although, prior to surgery or in case of severe hemorrhage, cryoprecipitate or intermediate-purity Factor VIII concentrates will be required.

4. The need for specific replacement therapy can be prevented or reduced in haemophilic or vWD patients requiring dental surgery, circumcision, and other forms of minor surgery, by using anti-fibrinolytic agents, such as tranexamic acid or epsilon-caproic acid.

5. Inhibitors of Factor VIII/ IX in haemophiliacs appear to be determined by genetic factors, rather than the type and dose of replacement therapy employed. They occur more frequently than was previously thought, in some 23% to 28% of cases.
Fortunately, about half of these cases are relatively low-titre inhibitors which do not usually develop anamnesis, and may be overcome.

High-titre inhibitors are much more serious. They are difficult and very costly to manage, either with large, tolerising doses of Factor VIII/IX; by employing Factor VIII inhibitor by-passing activity agents (FEIBA) such as PCCs, a PCCs, recombinant F.VII.a, or purified animal F.VIII preparations (Spey wood).

Commonly, a combination of these forms of treatment will be called for in managing acute hemorrhage, or in preparation for surgery. Only highly-specialised centres with good laboratory support are likely to succeed in handling the most serious, cases.