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**RARE BLOOD. AN UPDATED REPORT FROM THE  
INTERNATIONAL SOCIETY OF BLOOD TRANSFUSION  
WORKING PARTY ON RARE BLOOD DONORS.**

**Short Title:           Rare Blood Donors**

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**Glossary of Abbreviations:**

ALT	Alanine aminotransferase activity
EDTA	Ethylenediaminetetra-acetic acid
HIV Ag	Human Immunodeficiency Virus antigen
HTLV-I	Human T cell Lymphotropic Virus
IATA	International Air Transport Association
IBGRL	International Blood Group Reference Laboratory
IDP	International Donor Panel
ISBT	International Society of Blood Transfusion
NAT	Nucleic Acid Amplification Test
SCARF	Serum, Cells and Rare Fluids
WHO	World Health Organisation

## **Introduction**

International co-operation is often needed to ensure that blood of rare phenotypes can be made available to specified patients. The ISBT Working Party on Rare Blood Donors was developed to facilitate this process and to provide operative guidelines for blood services.

The Working Party has met regularly at ISBT meetings since 1984 and has conducted surveys and interviews of appropriate experts. The first published report of the ISBT Working Party was in 1999<sup>1</sup>. It outlined the history and workings of the WHO IDP and important information that has provided a basis for the effective exchange of rare blood between countries. Since that time, numerous changes and additions to procedures have taken place and these are documented in this updated report.

### **The WHO IDP and its usage**

In 2004 over 4000 donors from 60 centres in 26 countries were listed on the IDP. However these donors are not always dedicated solely to IDP use and may donate on a routine basis. Sometimes these donations may be frozen. It thus follows that some donors listed may not be available to give fresh blood, if they have donated blood recently.

Current rare donor categories are listed in Table 1 although some phenotypes are in very short supply.

Some reference centres may have antisera and monoclonal antibodies available for screening for rare donors. Supplies and advice can be obtained by direct negotiation with these centres. A further source of supply may be through the SCARF exchange Program (See: [jove.prohosting.com/~scarfex/](http://jove.prohosting.com/~scarfex/)) for details regarding membership of SCARF.

If a donor with a rare phenotype is found, the details including full phenotypes can be submitted, to the IBGRL and/or to the Rare Donor Programme in their own country. The IBGRL can confirm antigen typings on rare donors if necessary. The clinical significance of blood group antibodies varies<sup>2</sup>, even within a specificity, and this should be taken into consideration when utilizing the IDP.

Internet access to the IDP can be made at [www.bloodnet.nbs.nhs.uk/ibgrl](http://www.bloodnet.nbs.nhs.uk/ibgrl). A user name and password, obtainable from the IBGRL, is required to conduct a search procedure. The IDP gives details of all donors within a particular rare category, full phenotypes, panel code number, contributor's identification number, where the donor is based and whom to contact for donor availability. Users can then liaise directly with the appropriate centre to obtain blood. Contact details for the IDP for non-internet users are shown in Table 2.

### ***Arranging and making contact with rare donors***

The usual procedure to obtain blood for a difficult-to-transfuse patient is initially by contact with the local donor centre, then the State, Province, Regional or National Reference Centre, followed by reference to the IBGRL which holds the data on the WHO IDP.

Once possible donors have been selected from the IDP, the next step is to contact the authorised staff of the service where the donor is located. At this time, the availability of the donor(s) is ascertained, the urgency of the need assessed, and arrangements made for transport and financing. As different

countries have differing tests and standards for their accreditation of blood donors, it is important that these matters be fully discussed. For instance, national infectious disease testing requirements may differ between countries and thus preclude the acceptance of blood by the requesting centre. As transport regulations change from time to time between countries, the sending and receiving countries should clarify any such issues prior to the forwarding of the rare blood units.

### ***Standards for rare donors***

All institutions that contribute to the IDP should comply with their national standards for the selection of blood donors as this protects both the donor and the recipient. Blood should only be drawn from donors who meet these standards. Exceptions might be made in an emergency, where the recipient's life is threatened if blood is not available. These exceptional conditions must not endanger the donor. In such cases the patient's physician, the donor and the collection centre physician must agree to these exceptions and the agreement should be documented. Donors who are no longer acceptable for donation, because of residence/travel in certain geographical regions, should still be kept on the IDP and may later become eligible for donation if such restrictions should change.

All routine testing on the donor serum sample should be performed using reagents licensed in the country in which the blood is drawn, according to the manufacturer's directions and should meet all standards required in that country. Records of all testing performed on these donors should be kept up to date and should be easily available and interpretable.

### ***Frozen blood***

There are numerous centres that store frozen blood from donors with a rare phenotype. Some details of national organisations are noted in Table 3 but the list is incomplete. There are also many other national and regional blood centres that hold stocks of rare blood that are not listed on the IDP.

At such centres, units of red cells from donors with rare types are stored either by the low glycerol technique in liquid nitrogen, or in a higher concentration of glycerol, by mechanical refrigeration. The advantage of this stock is that the units are directly available without the need to contact specific donors. Many of these centres store rare units for national use but in special situations may release blood internationally. Special negotiations need to be made to ensure such blood can be forwarded rapidly particularly when it is required to be thawed prior to transportation. If blood is shipped in the frozen state, the instructions for thawing must be forwarded to the receiving centre.

Some countries have established expiration dates for frozen blood. Usually a dating of 10 years from collection is used, although rare blood, if stored at very low temperatures, can still be clinically effective well after the stated expiry date. If acceptable to the authorized officer of the receiving institution, frozen blood of any date may be used. The expiration date of the blood frozen by the Haemonetics ACP 215 has been extended to 10 years. Dating may be variable between countries, e.g. in the USA it is currently 3 years.

### ***Infectious disease testing for rare donations***

All blood utilized for international transport should have been fully tested for appropriate disease markers in the country of origin.

Because donor eligibility and testing requirements differ from one country to another, donor blood drawn in one country may not be suitable for transfusion in another. For example, HTLV-I, HIV Ag, Anti-HBc, ALT and NAT testing may not be performed in all countries. Additional testing may therefore be needed in the recipient country, especially for infectious diseases. Serum or plasma samples to be used for testing by the receiving centre should accompany the transport of any rare frozen/liquid unit of blood. Alternatively, if countries have very similar minimum testing programmes for transfusion transmitted infections, rare blood units may be exchanged without delay but after appropriate consultation with the receiving centre.

The serum or plasma samples to be forwarded should be at least 1-2 ml in volume and be clearly labeled with the number that links it to the blood unit . If the specimen contains an anticoagulant this should be indicated in the documentation. EDTA is the least acceptable anticoagulant, as the plasma cannot be used for all types of testing.

The samples should not have been stored at for more than 4 days at + 2 °C to + 8 °C prior to freezing at -20°C or lower. Frozen test samples need to be kept at -20°C or lower, and liquid samples at +2<sup>0</sup> to +8°C during shipment. When fresh units less than 4 days old are being shipped, the samples may be kept more conveniently at +2<sup>0</sup> to +8°C.

When new infectious disease screening tests are introduced to a laboratory, these tests should be retrospectively applied to the serum samples. These results should be documented and be readily obtainable to ensure that the stored unit can be quickly released for clinical use. It is also appropriate to re-

test a fresh blood sample from the rare donor.

### ***Documentation of the Rare Donation***

The collecting centre must include specific information with each shipment of rare blood. This documentation should include

- the full results of infectious disease testing, and where possible, the name of the manufacturer of the infectious disease tests performed.
- the date the donor unit and sample were drawn,
- the unique identification number
- the collecting centre's name
- full details of ABO, Rh and other typings performed on the rare unit

### ***Transport and reimbursement requirements for rare blood***

Although some blood centres may be able to absorb the costs involved in transport of rare blood, it should be a principle that the receiving centre should cover all costs of the blood received. The charge made to the receiving centre for the blood unit itself should not exceed the cost that would be paid within the sending country. The receiving centre should cover the costs of transportation, insurance and any other miscellaneous expenses. If additional blood typing or disease testing at the donating centre is required, these costs should also be invoiced to the receiving centre, but only after agreement of both parties.

Financial arrangements should be discussed at an early stage to ensure that there are no misunderstandings. Modern communications mean that such negotiations can be done quickly, but bureaucracy should never be allowed to impede the clinical needs of patients.

## **Transport of blood requiring refrigeration.**

### *1. Containers*

Insulated and leak-proof boxes are now commercially available for the transport of blood at + 2 °C to + 8 °C. In general, the thickness of the insulation, which is usually polystyrene, determines the length of time in which blood can be stored at the appropriate temperatures. The type of box selected should have been tested under the environmental conditions to which it may be exposed.

Prior to packing, blood and the box should be reduced to a temperature of + 2 °C to + 8 °C. Blood should then be packed in outer leak-proof plastic containers. Inserts of melting ice are then included, with the volume of the ice being at least equal to the volume of the blood being sent. Commercial packs containing coolant are available or alternatively, ice sealed in metal, glass or plastic can be utilized. Leakage must be avoided. Absorbent material equivalent to the volume of the transported blood plus coolant in the box will obviate unexpected problems of leakage. If ice has been frozen to a very low temperature, it should be thawed to melting point before the blood is packed. No ice insert should be in direct contact with the blood unit. It should be packed on the sides and top of the container to achieve best maintenance of a cool environment. Once the blood is packed, the top of the container should be sealed tightly.

### *2. Temperature*

A continuous temperature-measuring device, such as a "data logger", should be included in each consignment of rare blood. These low cost electronic

temperature recorders securely store temperature information, which remains available for downloading to a computer even in the event of battery failure or removal. These are relatively cheap and provide information on the temperature control of the blood units during transportation. If these are not available a “maximum-minimum thermometer” should be included, but are much less satisfactory.



### *3. Transport of frozen blood*

To transport liquid nitrogen, low glycerol frozen cells, use of specifically designed blood shippers is required. Commonly, such blood units are thawed prior to transportation. Due to the potential risk of contamination, consequent on using ‘open’ freezing and thawing procedures in clean rooms, these thawed units may have only a shelf-life of 24 hours and this greatly limits the time available for international transportation. Newer ‘closed’ methods of freezing and thawing units utilizing modified apheresis machines and sterile docking procedures have extended the post thaw expiry time to up to 14 days at some frozen blood banks and these should be used wherever possible.

It is easier to ship cells frozen by the high glycerol technique as these units can be stored on ‘dry ice’ (solid carbon dioxide) Sufficient ‘dry ice’ must be placed in the insulated containers to ensure temperatures are maintained for the total (door to door) time of transport. As a guide, for international flights of 36 hours, 10-15 kg of dry ice is required although this varies depending on the type of outer container used. Frozen packs may be very fragile and can be easily damaged. The container of the frozen unit should be securely placed to prevent movement once some of the dry ice evaporates. ‘Dry ice’ may need to be added during shipment to ensure temperatures are maintained and this must be arranged in advance with the shipping agents.

All containers used for the transport of frozen blood should be initially validated for their ability to maintain low temperature storage for the required time periods.

Blood centres forwarding frozen blood to another centre should ascertain that the receiving centre has validated facilities for de-glycerolisation procedures as well as personnel able to perform this task. The procedure for de-glycerolisation should be sent with the blood unit to the receiving centre. International shipment of frozen units stored on dry ice can be arranged by specialist couriers skilled in the transport of frozen biological goods. However shipment may take longer than for units stored at +2-8°C.

#### *4. Documentation and labeling of containers*

There is no mandated uniform method of labeling rare blood for international transportation. However, to avoid any possible confusion, legible and concise documentation on both the airway bills and the consignment, is essential at all stages from the initial request to the final dispatch and receipt.

The following documents are necessary and a copy of each should be faxed to the receiving centre and/or the freight-clearing agent prior to the arrival of the blood.

(a) A covering sheet/fax. This document should be faxed even if the information has been sent by e-mail. All the flight details including the departure and arrival times of the flight, and the carrier used, should be clearly specified. The airway bill number must be provided to the receiving organisation to permit tracing of the consignment.

(b) Airway Bill

Each airline has a specific Airway Bill form. The wording on the Airway Bill is very important and it is useful to place additional information on the document for clarity e.g. Medical emergency-Blood for urgent transfusion, Perishable/Urgent etc.

(c) The Airport of destination should be specified by both name and International code. The Handling Information Instructions area should be fully completed and include any special appropriate instructions e.g. REFRIGERATE AT 2-8°C ; DO NOT FREEZE; PLEASE PHONE CONSIGNEE ON ARRIVAL CONTACT NUMBER.....

(d) Invoice for customs purpose. A nominal value of \$10 is suggested.

(e) A Safety Certificate may be required in some countries. Check with the airline to assess if this is needed

(f) Some countries have very strict requirements for the importation of blood and specific documentation may be required. If the country of the consignee requires a special permit it is advantageous to supply a copy of the permit with the documentation for each consignment sent and not just quote the permit number.

(g) It is recommended that all rare blood have placed on the container large labels stating "RARE BLOOD (HUMAN)" and the temperature at which the box is to be stored when not being transported. Similar information must also be recorded on the Airway Bill in the section marked "Handling Information". The labels should also have the full address, telephone and fax number and contact person at the receiving laboratory.

(h) It is also important to document on the container an "out of hours" phone number, to be contacted in case of delay in blood transport. Full details of the consignee should also be included. It is recommended that the box be of a distinctive colour or type to enable rapid recognition by handling

staff.

(i) The box should be labeled as “NON-INFECTIOUS” and be clearly labeled as URGENT.

### ***Airline arrangements for rare blood transportation***

The international transportation of blood usually means that special arrangements need to be made to ensure there are no delays. Close contact with specific airlines, customs agents and airline staff can usually facilitate the efficient transfer of blood between countries. There is commonly a good sense of co-operation and media attention that sometimes can assure that all systems are favourable for blood transportation. Where a Courier company is used, the significance of the consignment must be explained and the need for special arrangements to ensure the most rapid delivery of the blood units.

When determining the route by which blood should be transported, airline routes should be chosen that ensure the blood is transported with the minimum of time, but arriving at times that are suitable for the receiving laboratory. Consignments of blood arriving late at night may be mislaid.

The consignee should inform by fax, telephone or email details of the airway bill to the receiving laboratory. Poor communications are not infrequently the cause of blood consignments being mislaid. The name and phone number of the person who will receive the shipment should be displayed on the outside of the container.

Centres should ensure that blood being forwarded to another centre does not arrive on a public holiday as this may cause major delays in delivery. Close

consultation between centers is required to obviate this problem.

### ***International Air Transport Authority (IATA) regulations***

The transport of blood must be according to IATA Dangerous Goods regulations which are contained in their handbook, published regularly with amendments (3) With frozen blood, stored in dry ice, there may be local rules concerning shipment and these should be checked with the relevant airlines.

Blood is classified as a “biological product” under Section 3.6.2.1.3 and its classification is covered in Section 3.6.8. Blood to be transported must be tested for infectious agents prior to transportation and if the blood units are non-reactive, the blood can be categorised as “known not to contain pathogens”, in which case there are no specific packing requirements or instructions required by IATA. However, it is recommended that the general packing requirements of packing instructions 650 (a) and (b) should be observed, particularly in regard to leak-proof containers, watertight secondary packaging and absorbent packaging.

### **Discussion**

To provide for the safe transport of precious rare blood both within and between countries, it is recommended that these guidelines be incorporated into the Standard Operating Procedures of individual blood centres.

The ISBT Rare Blood Working Party members are available to answer queries regarding matters related to rare blood. The IDP also welcomes input and particularly clinical details of rare blood transfusions carried out internationally. The IDP invites blood centres to send details of blood donors who could be eligible for inclusion on the rare donor list and can also provide facilities for verification of their rare donor status.

Finally, it is recommended that countries carry out surveys of their need for

rare blood and to determine their exact requirements based on clinical requirements.<sup>2,4,5</sup>, The provision of rare blood is an expensive therapy and blood centre budgets should make due allowance for the costs involved.

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**Table 1** Categories of rare phenotypes currently listed on the IDP.

Phenotypes	
O <sub>h</sub>	Jk(a-b-)
CDE/CDE	Di(b-)
CdE/CdE	Yt(a-)
C <sup>w</sup> D-/C <sup>w</sup> D-	Sc:-1
-D-/-D-	Co(a-)
Rh <sub>null</sub>	McLeod
Rh:-51	Vel-
LW(a-b+)	Ge-
LW(a-b-)	Lan-
S-s-U-	Lan(+)
S-s-U(+)	Jo(a-)
pp	Gy(a-)
P <sup>k</sup>	Hy-
Lu(a+b-)	At(a-)
Lu(a-b-)	Jr(a-)
Kp(a+b-)	In(b-)
Kp(a-b-)	En(a-)
Js(a+b-)	Cr(a-)
K <sub>o</sub>	Er(a-)
K:-11	Ok(a-)
Fy(a-b-)	JMH-

A limited number of hr<sup>S</sup>- and hr<sup>B</sup>- (Rh:-34) donations are available from the South African Rare Donor File

**Table 2** Contact details for WHO IDP staff

Contact Name	E mail address	Telephone	Fax
Joyce Poole	joyce.poole@nbs.nhs.uk	+44 117 991 2105	+44 117 959 1660
Jackie Banks	jackie.banks@nbs.nhs.uk	+44 117 991 2106	+44 117 959 1660
Out of hours	Ask for IBGRL staff to be paged	+44 117 991 2000	

**Table 3** Details of some International and National Frozen Blood Banks

<b>Program</b>	<b>Blood Bank</b>	<b>Website (URL) and Email addresses</b>	<b>Method of Freezing</b>
American Rare Donor Program	ARC Philadelphia, USA	snance@usa.redcross.org achurch@usa.redcross.org ardp@usa.redcross.org	High Glycerol
European Frozen Blood Bank Council of Europe	Sanquin Amsterdam, NL Holland	www.sanquin.nl M_Overbeeke@sanquin.nl Europeanbloodbank@sanquin.nl Phone 31 20 5123373	Low Glycerol
French Rare Donor Program	CNRGS, Paris, France	Phone (24 hrs): 33 1 55 25 12 12 Fax: 33 1 55 25 12 03 cnrgs@ints.fr	High Glycerol
German Rare Donor Program	DRK BSD, Ulm, D Germany	www.uni-ulm.de/~wflegel/RARE/ w.flegel@blutspende.de	High Glycerol
Japanese Rare Donor Program	Japanese Red Cross, Osaka, Japan	tani@osaka.bc.jrc.or.jp	High Glycerol
South African Rare Donor File	SANBS ECR Pinetown, South Africa	<a href="mailto:smarte@ecr.sanbs.org.za">smarte@ecr.sanbs.org.za</a> Fax +27 31 7084636	High Glycerol
UK National Blood Service Frozen Blood Bank	National Blood Service, Edgbaston, Birmingham, UK B15 2SG	Frozen.bank@nbs.nhs.uk	High Glycerol



