

ISBT WORKING PARTY FOR RARE DONORS

24 YEARS OF INTERNATIONAL COLLABORATION

In 1984, in recognition that global cooperation is essential to transfuse patients with rare blood needs when a domestic product is not available, the ISBT Working Party for Rare Donors was formed.

Terms of Reference, ISBT Working Party for Rare Donors

- To develop guidelines for standardization of listing, labeling, shipping, testing and reimbursement for rare donor blood
- To provide a centralized international web resource for providing ongoing information on matters related to rare donors

- To develop and extend the liaison with the International Blood Group Reference Laboratory (IBGRL in Bristol, UK) and thus assist blood services internationally to support and contribute to the WHO International Rare Donor Panel.

Term of Reference #1 was addressed by a publication in 1999 and an updated white paper in 2004 posted to the ISBT website in the Working Party for Rare Donors section. This paper is a must read for those faced with the challenge of importing or exporting rare blood products, especially for those facilities who seldom have this need. It addresses topics such as the WHO International Donor

Panel (IDP) and its use, arranging and making contact with rare donors, standards for rare donors, frozen blood, infectious disease testing, documentation of the rare donation, transport and reimbursement requirements, transport of blood requiring refrigeration, airline arrangements for rare blood transportation, and International Air Transport Authority (IATA) regulations,

The Working Party realized the importance of efficient, effective communication especially with those for whom the presentation of a patient with a rare blood need requiring national or international shipment of the product is a once in a lifetime career occurrence.



Meeting of the Working Party in South Africa in 2006. Formal meetings are held at every ISBT Congress and informal meetings at the regional congresses. There are currently 118 facilities affiliated with the Rare Donor Programs across the world, many of them have not only rare donor programs but also type for common antigens whose absence in combination with other antigens can make the blood difficult to find. Effective communication between programs is critical to success.

Members of the WP

Chair	Sandra Nance	USA
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	Joyce Poole	UK	Vered Yahalom	ISRAEL
	Marie Lin	TAIWAN	Willy Flegel	GERMANY
	Marijke Overbeeke	NETHERLANDS	Tani Yoshihiko	JAPAN
	Marion Reid	USA	Zhu, Ziyang	CHINA
	Pauline Fogg	SOUTH AFRICA		

Term of Reference #2. A flow chart has been prepared by the WP: available on <http://www.isbt-web.org/images/flow-chart.gif>, which is helpful in showing the pathway that is followed when rare blood is needed either domestically or internationally. This is one of the ways

the WP has addressed Term of Reference #2. This flow chart has also been presented whenever possible to scientific audiences to ensure the knowledge is shared to enable an efficient process when rare blood is needed.

Term of Reference #3 is an on-going charge to the Working Party members to ensure that international collaboration is a top priority to meet transfusion needs. A recent review of international requests to the WHO IDP gives insight into the rarity of the requests.

Outcome of Rare Requests to WHO International Donor Panel - August 2004 to August 2006			
INTERNET REQUESTS			
Australia	4	Switzerland	30
Denmark	12	The Netherlands	25
Canada	3	Philippines	30
France	6	UK	351
Czech Rep	18	USA	20
Germany	34	Total	596
Israel	27		
Norway	2		
Poland	11		
Portugal	2		
Scotland	8		
Sweden	13		

Outcome of Requests to WHO International Rare Donor Panel			
COUNTRY	RARITY	UNITS	OUTCOME
UK	Pk	2 frozen UK	Good
South Africa	Kp(b-) rr	2 local 2 sister	Good
Israel	Oh rr	1 South Africa	Baby died
UK	Rh:-51	2 UK, 2 Finland	Good
Brazil	Kp(b-)	6 USA frozen	4 given, pt died
Saudi Arabia	Ko	1 auto + EPO	Good
Australia	Vel -	10 country, 1 Canada	Patient died
Sweden	En(a-)	6 Japan	Good

- Additionally, Vox Sanguinis is conducting a world-wide survey of Rare Donor Programs across the world that is expected to give additional insight into which rare requests are not able to be met within the country. This will provide an impetus for further collaboration and measurements of success as well as indicate selective screening for antigens needed in each responding country.
- Another measure of success is the condition of the units when they arrive at their destination. The Working Party has created a tracking form, the Rare Blood Shipment Form, to allow quantitation of success. Please see below for website address where the form can be found. This form has been translated and implemented in Germany. The results will be presented at the ISBT Congress in Macao 2008. This will provide useful information for global implementation in other countries besides Germany.
- The working party has regular formal meetings, which are held at each Biannual Scientific Congress of the ISBT. In addition, the working

party organized programs on rare blood at the 2002, 2004, and 2006 ISBT Congresses and there were Rare Donor talks at the Hanoi Regional Congress in 2007 and will be in Macao in 2008. The working party has also participated in World Blood Donor Day by presenting case studies in which it has been necessary to obtain blood via a rare donor panel.

These educational programs have helped to raise the awareness of the wider transfusion medicine community about the importance of availability of rare blood.

http://www.isbt-web.org/members_only/society/working_parties.asp

Rare Types Available in South Africa

Bombay Oh	k-negative
Co(a-)	Kn(a-)
Do(a-)	Kp(a+b-)
Ge-negative	Lan-negative
Rh:-34	Lu(b-)
hrS-negative	Rg(a-)
Hy-negative	Rhnull
In(a+b-)	U-negative/variant
In(Lu)	Vel-negative
Jk:-3	Yt(a-)
Js(b-)	

SOUTH AFRICA

The South Africa Rare Donor Program was established originally to meet the needs of patients in South Africa who have developed antibodies to high frequency blood group antigens. In a multi-ethnic community such as South Africa, the frequencies of the different blood group antigens vary significantly between the Black, White, Indian and Mixed Ethnic Origin populations and it is necessary to have a range of rare type blood available. Rare donors are identified by actively screening selected population groups using rare reagents and by family studies. A total of 26 rare type categories are listed on the South African

rare Donor Panel, and within each category one or more different additional phenotypes are available. The rare donations are available upon request from the central Rare Donor low temperature frozen storage unit in Durban, South Africa. Contact Pauline Fogg at: foggp@ecr.sanbs.org.za if further information is needed.

**Pauline Fogg
Elizabeth Smart**

South African National Blood Service ■

WHO INTERNATIONAL RARE DONOR PANEL

The WHO International Rare Donor Panel (IRDP) was set up following a recommendation made by the ISBT in 1964. The first lists were dispatched on March 21st 1968 and included nearly 300 donors from 10 countries. Since that time the day to day running and organization of the IRDP has been carried out by the red cell reference department of the International Blood Group Reference Laboratory (IBGRL), originally in London and now in Bristol, UK. The role of the IBGRL is to compile information on rare donors that have been identified at other centers around the world and to make this information available when rare blood is needed. There are currently > 4000 rare donors listed from 60 centers in 26 countries.

The IRDP is maintained through screening programmes undertaken at blood centers around the world. The NHS Blood and Transplant South London Centre has been screening for rare donors for > 30 years and provides more rare donors in the UK than any other centre. Screening programmes are also carried out in the USA, Japan, China, and South Africa and in several European countries. The Japanese Red Cross provide many donors for the IRDP and these include certain rarities such as Di(a+b), Jr(a-), D-/D-- and KO which are in short supply in other parts of the world. We work in close collaboration with the American Rare Donor Program which also provides a large number of donors for the IRDP. One of the problems in IRDP maintenance is the shortage of some rarities e.g. Rhnull, D-/D--, hrS-, Co(a-b-), Lan, KO, Sc:-1,-2,-3 and McLeod phenotype. Another is the lack of availability of resources for screening programmes to be undertaken in more centers. Requests for rare blood are received from all over the world and blood provision can be especially difficult when a specific ABO group is required and/or multiple antibodies are present in the patient's serum.

To summarize, the IRDP has evolved over the past 40 years and enables the effective exchange of blood between countries. This international co-operation ensures that blood is made available to specified patients, even those with the rarest of blood groups. Access to the IRDP is available to authorized users via the Bristol Institute for Transfusion Sciences/IBGRL website:

www.blood.co.uk/ibgrl

A user name and password are needed to conduct a rare donor search and these can be obtained from

joyce.poole@nbs.nhs.uk

or nicole.warke@nbs.nhs.uk

Joyce Poole

International Blood Group

Reference Laboratory

National Blood Service ■

FRANCE

A national database including both donors and patients with a rare blood phenotype was implemented in France in the 1960s, which currently enlists 9750 people.

A national rare blood bank was further set up, presently including 5550 cryopreserved RBC units (-80°C) from 1631 blood donors. Between 1994.01.01 and 2008.03.12, 2065 RBC units were delivered (315 patients, 843 transfusion episodes); 33% were transfused to sickle cell patients and 4% shipped abroad.

Pierre-Yves Le Pennec

Centre National de Référence pour les

Groupes Sanguins

Institut National de la

Transfusion Sanguine ■

ITALY (in particular, Region of Lombardy)

In Italy, some centres routinely type blood donors for a number of antigens and hold frozen inventories of rare RBC units. Although the country still lacks a national rare donor program, its blood authorities are working at the establishment of a countrywide network of dedicated centres. The only large and institutionalized program to date is the Rare Blood Components Bank for the Region of Lombardy, which started operations in January 2005 at the Milan Polyclinic Hospital. The Bank typed 37,382 donors in its first 3 years, identifying 5,542 rare donors and collecting 3,795 rare blood units. This blood transfusion centre has managed a rare donor programme for the Region of Lombardy (Italy) since 2005. The programme, named "Rare Blood Components Bank - Reference Centre for the Region of Lombardy", is the only one of its kind in

Italy and it has already reached a remarkable size. Rare donor data are collected in the general blood donor database which is used all over the Region, and a regional bank of fresh and frozen rare blood units has also been set up at the facility and will be greatly expanded over the next three years. The immunohaematology laboratory is a reference laboratory for cases of complex red cell immunisation. While this programme serves mainly the Region of Lombardy, its services are open to blood transfusion centres countrywide and all over the world. As an AABB-accredited Immunohematology Reference Laboratory, our facility is also a member of the American Rare Donor Programme (ARDP), and an adequate supply of rare antisera is ensured by our participation in the SCARF Exchange.

Nicoletta Revelli

Antonietta Villa

Centro Trasfusionale

di Immunoematologia ■

THE NETHERLANDS

In the Netherlands, Sanquin Blood Supply has an inventory of frozen high-frequency antigen (HFA) negative RBC available (Sanquin Bank of Frozen Blood, formerly known as the Blood Bank of the Council of Europe). In the Netherlands, all donors are typed for DCcEe, and for k if K-positive, hence fresh donor units with rare Rh phenotypes or k-negative can be made available. A limited HFA donor typing programme has been conducted, and for example Vel-, Lu(b-) Co(a-), Kp(b-) donors have been identified. Future typing programmes will focus on identification of U-negative donors.

Masja de Haas

Marijke Overbeeke

Sanquin, Research at CLB and Sanquin,

Diagnostic Services ■

ISRAEL

The Rare Donor Program in Israel is one of the major activities of our National Blood Group Reference laboratory since 1970. Over the years we have encountered many Rare Donors, which include, Oh (Bombay), p (Tj(a-), Pk, K:-22, KO, Dr(a), Lu(b-), Lu:-20, LW(a-) Yt(a-), Lan neg, Jr(a-), Ge:-2,3, Ge:-2-3, Au(b-) Raph neg, AnWj neg, Vel neg, and ABTI neg. To encourage these Rare Donors to donate, we have organized two meetings which have been very successful. They have taken place in the Blood Center of Magen David Adom, and have included lectures and social activities. In



addition, we have had one or more Rare Blood Donor give a talk about their personal experiences. Our Rare Donor Program meetings are active and ongoing, and we intent to continue them as they are very important to our services in Israel.

The Immunohematology staff, including Vered Yahalom, Cyril Levene and Orna Asher, and all of the workers involved with the working up of the material of the rare donors.

**Vered Yahalom
Cyril Levene
Orna Asher**

National Blood Services ■

UNITED STATES OF AMERICA

The American Rare Donor Program (ARDP), a cooperative program of AABB and the American Red Cross, was formed in 1998 when the rare donor databases of the two organizations were merged. Since that time the ARDP has grown to a membership of 81 immunohematology reference laboratories with a database of approximately 38,000 active rare donors. Members screen blood samples from donors and submit phenotype information on rare donors to the database. The database is housed in Philadelphia where ARDP personnel receive faxed requests for rare blood components from the ARDP members. The database is searched for registered donors of the requested phenotype. When such donors are found, members with these donors are contacted via fax to determine the availability of units.

The ARDP defines a rare donor as a donor who meets one of the following criteria:

- Lacks a high-prevalence antigen, those that occur in less than 1 in 1000 donors
- Lacks multiple common antigens; the donor must be group O or group A and meet one of the following sets of criteria:

- Set 1: R1, R2, RO, or rr AND K:-1 AND Fy(a-) or Fy(b-) AND Jk(a-) or Jk(b-) AND S- or s-
- Set 2: R1, R2, or rr AND K:-1 AND Fy(a-b-)
- IgA deficient, having IgA of a level < 0.05mg/dL tested on samples from two separate draw dates

Currently the ARDP has approximately 3700 donors whose RBCs lack a high-prevalence antigen, 34,000 donors whose RBCs lack multiple common antigens and 200 donors who are IgA deficient. The large database of multiple common antigen-negative donors serves the needs of patients with sickle cell disease; requests for these patients account for approximately one-third of ARDP requests.

The ARDP has filled approximately 95 percent of its requests using rare donors who are registered in the ARDP or from international counterparts. From January 2005 to December 2007, 2287 requests were received; 2139 of which were filled or partially filled; 148 were unfilled.

The ARDP imports and exports rare units through the WHO International Rare Donor Panel as well as other international rare donor registries. From January 2005 to December 2007, the ARDP imported a total of 20 rare units from the South African National Blood Service, the National Blood Service in the UK, and the Japanese Red Cross. During this same time period, the ARDP exported a total of 48 units to 7 countries.

Current challenges to the ARDP include the decrease of reagent availability especially for antigens of low prevalence such as Jsa and V, breakage of frozen rare units during shipping, computer incompatibilities between member facilities as members transition to ISBT labeling of blood components, and inability to serologically predict compatibility when certain variant antigens are present such as hrB and hrS; these

cases require DNA testing to select appropriate donors.

**Cynthia Flickinger
Sandra Nance
Geraldyn Meny**

ARDP Advisory Committee
American Rare Donor Program ■

The ARDP can be accessed through ardp@usa.redcross.org, the program's manager, Cynthia Flickinger at flickingerc@usa.redcross.org or the director, Sandra Nance at snance@usa.redcross.org

SÃO PAULO, BRAZIL

Despite some initiatives developed in Brazil, until now there is not a Brazilian national panel of rare donors, even though a few blood centers have their own donor panels. At Hospital Sirio Libanes Blood Bank, our rare donor panel has archived the following phenotypes: KK: 93; Kp(b-): four; Di(b-): nine; IgA deficient-donors: 28; Vel-: 13; r₁r₁: four; r₁r₂: four; McLeod: two. In addition, we also have the following phenotypes in our frozen red cell bank: McLeod (14 units); Vel- (4); Di (b-) (4); Kp(b-) (18); KK (18); IgA deficient (3), ryry (1); r₁r₁(1); r₁r₂ (5).

Furthermore, a special stock of frozen red cells typed for RH, K, FY, JK, Ss designated for patients with multiple antibodies is available. In the last five years we had 10 patients with rare phenotype/antibodies (1 McLeod; 2 anti-k; 2 anti-U, 1 anti-Lan, 1 anti-Ku, 1 anti-Dib, 1 anti-RH17, 1 anti-Lub). We could provide blood from our stock for 4 (40%) of these patients (additionally, one of the patients also received more units from the International Blood Group Laboratory due to severe bleeding); one patient received blood from the International Blood Group Laboratory (Ko blood); one patient had a family member compatible for transfusion (Lan-); and the other 4 patients did not receive any blood transfusion (2 anti-U, 1 anti-RH17 and 1 anti-Lub). Therefore in the last five years we transfused 39 rare red cells from our stock whereas 26 frozen red cells had a rare phenotype [7 McLeod, 17 KK and 2 Di(b-)] and 13 had special phenotypes for patients with multiple antibodies.

We consider it important to increase our panel with a good number of U negative red cells, since recently we had 2 patients with anti-U with no red cells available. Another important phenotype that would be interesting to

have in our stock is RH:29- and RH:17. Because of the limited availability of rare units in Brazil, we count on the good relationship with the International Blood Group Reference Laboratory, located in Bristol, UK that was able to provide us five frozen red cells (three McLeod and two Ko) in the past 5 years.

As happens with other developing countries, our main problem relates to receiving compatible rare blood in a reasonable time for transfusion, especially when the blood is coming from a foreign center. Our customs are very rigid and bureaucratic, deeming it mandatory to present a number of documents, which sometimes hold precious rare units for days at the customs until release. Anyway, despite our local problems, we consider that this initiative should be maintained and supported as a global collaborative effort.

Silvano Wendel

Director Médico - Banco de Sangue
Medical Director - Blood Bank
Hospital Sirio Libanês ■

CHINA

Finding compatible blood for patients to meet the needs of rare blood transfusion, China developed a National Rare Blood Screening Program at 2005. The program was implemented to screen large numbers of donors for blood types. Implementation steps included obtaining broad community endorsement of the concept, educating blood center personnel, developing educational materials, developing a computer system to facilitate selection of donors to be test, doing the laboratory testing to identify rare blood and notifying the rare donors. Over 1,200,000 Chinese donors were screened their rare blood antigens by different serology methods as well as DNA typing. A monoclonal antibody preparation system has been established. Today over one thousand rare blood donors have registered in China Rare Blood Bank. To the end of 2007, 9 regional blood centers have added to this screening program. A center frozen storage facility was established in Shanghai. Five transgenic cell line have been established and two hybridoma have been produced which have the specificity of anti-GPA and anti-I, respectively. China rare donor program has an active program in place to provide rare blood for patients in need.

Ziyan. Zhu

Shanghai Blood Center ■

TAIWAN

There are 6 blood centers in the Taiwan Blood Services Foundation (TBSF). The frozen stocks of rare blood are kept in 2 centers with consolidated testing laboratories, the Taipei and Kaohsiung Blood Centers, with current inventory of more than 300 units. The Taiwanese rare blood donor files include: Fya- (0.3%), Fy(a-b-)($<1:10,000$), Jk(a-b-)($<1:5,000$), RZRZ, Rh null, s-, Para-Bombay, ABO subtypes except B3, i adult, KO, p and blood units negative for multiple common antigens. They were identified from routine work, and special screening projects using automatic Olympus PK analyzers.

Sujen Lin Tsai

Taiwan Blood Services Foundation ■

GERMANY, SWITZERLAND AND AUSTRIA

In the three German-speaking countries a network of more than 10 blood services is established that collaborate in diagnosis and supply for patients in need of rare blood. The three blood centers in Hagen, Munich and Ulm (all in Germany) maintain stocks of rare RBC units that are kept frozen in liquid nitrogen for up to 10 years. A deposit of frozen Swiss RBC units is kept in Amsterdam (the Netherlands) and of Austrian RBC units in Vienna.

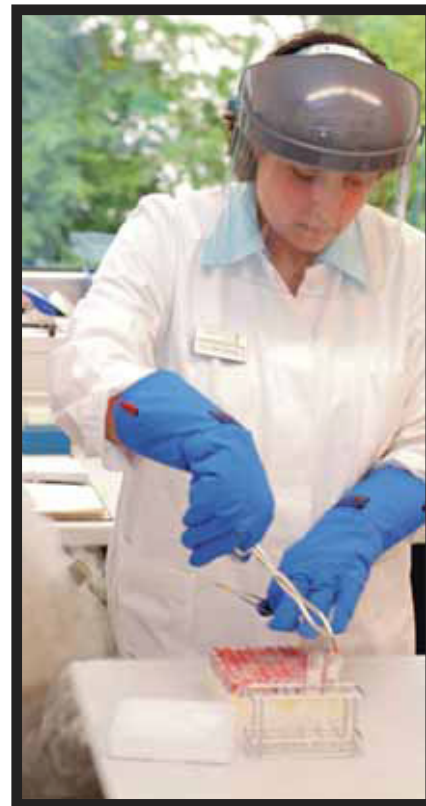
The supply with fresh RBC units for phenotypes like k negative, e negative or CCddee, which used to be a problem until the last decade, is now feasible in most cases. Patients in need of blood negative for the Kpb, Lub, Vel or Yta antigen can often be supplied with fresh RBC units, too.¹ Such RBC units are earmarked at most blood centers and kept on shelf until used as needed or transfused independent of their rare phenotype, if not frozen. Frozen stock is nevertheless required if higher numbers of RBC units are required. Moreover, it is an exception if fresh blood is available for rarer blood groups. For such patients stocks are hence kept as frozen RBC units, many of which remain in short supply today.

Since its foundation in 1998 the German Rare Donor Working Party has held regular meetings and maintains a dedicated website,² which is frequently used for current contact information retrieval. Meeting presentations are available online at this website in German/English. The Working Party contributes to the national conferences of the Deutsche Gesellschaft für Transfusion-

smedizin und Immunhämatologie (DGTI) and the Association Suisse de Médecine Transfusionnelle (ASMT/SVTM) as well as to professional journals.^{1,3} In 2005, the follow up of rare RBC unit supply and patient outcome was initiated using the ISBT report form (available online² in German and English). A first analysis will be reported at this year's ISBT International Congress to provide an overview on demand and supply for the various rare blood groups as well as the logistic difficulties.

Willy A. Flegel

Institut für Transfusionsmedizin,
Universitätsklinikum Ulm
DRK Blutspendedienst
Baden-Württemberg - Hessen ■



▲ Stocks of frozen red blood cells (RBC) are instrumental for the diagnosis and the supply with RBC units in patients carrying rare blood groups. The handling of RBC samples is shown that are stored on liquid nitrogen in the Blood Group Reference Laboratory at the Institute of Clinical Transfusion Medicine and Immunogenetics Ulm.

References

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3. <http://www.uni-ulm.de/~wfllegel/RARE/DOK/Haemotherapie2004SeltBlut.pdf>