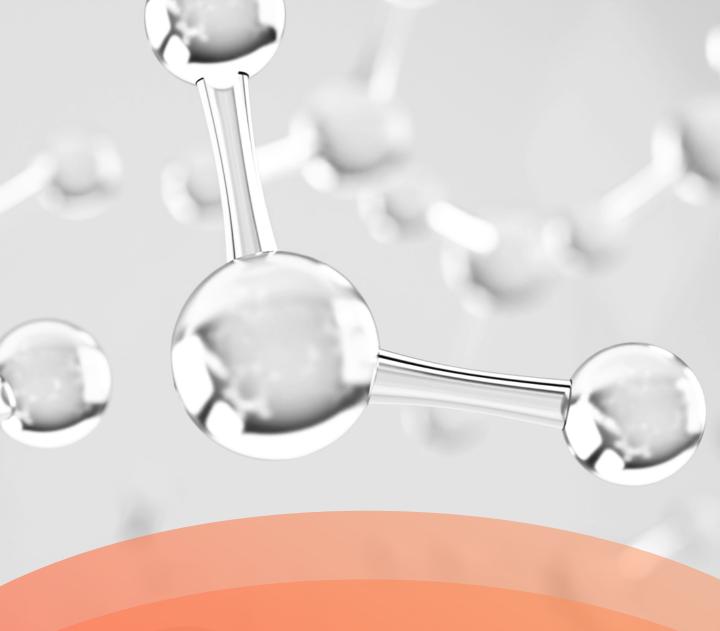
Annual Report REDMO





Published by:

Josep Carreras Leukaemia Foundation - REDMO

Iconography: Freepik, Noun Project

Images:

Design:

aliamc@grafika.help

Correction and translation:

Spanish population data:

Instituto Nacional de Estadística

Country population data:

Wikipedia

International activity data:

World Marrow Donor Association – Global Trend Report 2020





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REDMO Bone Marrow Donors Registre

In 2021, we celebrated the 30th anniversary of the REDMO Bone Marrow Donors Registry.

This was certainly a very special milestone for all of us: three decades of so many people's dedication, hard work and effort.

Before the creation of REDMO, Spanish patients could only receive a transplant if they had a compatible sibling or relative, which only occurs in less than 30% of cases.

To rectify this situation, in 1991, with the help of Professor Ciril Rozman and Doctor Albert Grañena, we began to take the first steps towards creating a registry of unrelated donors in our country.

REDMO's development was fully accomplished in 1994, when it was integrated in the public healthcare network of the National Health System with the signing of the first framework agreement between our Foundation and the Ministry of Health. In 2021, we renewed this agreement, enabling us to guarantee the stability of our registry and giving us the opportunity to imagine and embrace new challenges.

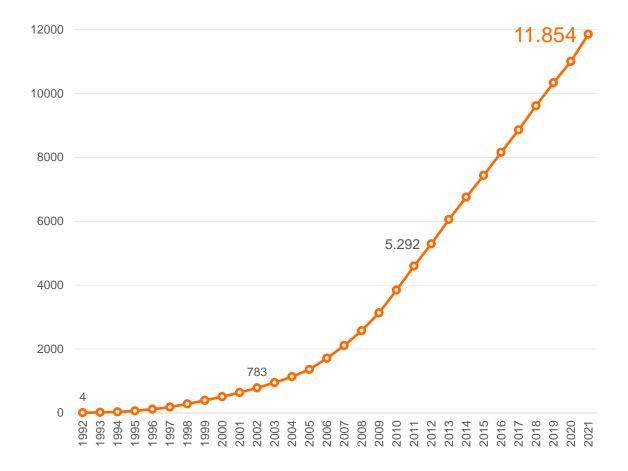
The framework agreement stipulates that REDMO is responsible for:

- Managing the database of Spanish donors: over the last 30 years, 517,949 unstoppable donors have registered on REDMO.
- Searching for compatible donors for Spanish patients: REDMO has initiated 16,261 searches, through which we have located at least 1 compatible donor for 15,426 patients. REDMO's searches are, for the most part, financed by the budgets of the public healthcare system. REDMO is the only program in Spain authorized to manage unrelated donors donating blood stem cells to patients treated in Spanish hospitals.
- Coordinating the transportation of bone marrow, peripheral blood and umbilical cord blood from the place of donation to the transplant hospital. Over the last 30 years, REDMO has made it possible for 11,854 donations to reach the patients who needed them. Of these donations, 8,166 went to Spanish patients and 3,688 to foreign patients.

REDMO is the only donor registry authorized to obtain these stem cells from donors living in our country.









REDMO is connected to the international network of registries and, therefore, has access to all the voluntary donors and umbilical cord blood units available around the world. Moreover, REDMO receives the search requests issued by registries in other countries requiring a donor or umbilical cord blood unit from our country.

Over the course of REDMO's history, we have made substantial improvements, including:

- The computerization of all the procedures.
- Quality control of all of the procedures.
- Contracting the staff required in each department to continue offering the fastest and most effective service possible, always in accordance with our quality standards.
- Ensuring the sustainability of the system.
- Adapting to the latest advances achieved in the world of transplantation.

Thanks to their dedication and wisdom, we now have a team and mature registry that oversees all the transplant activity and unrelated-donor haematopoietic progenitor cell donation in our public health system.



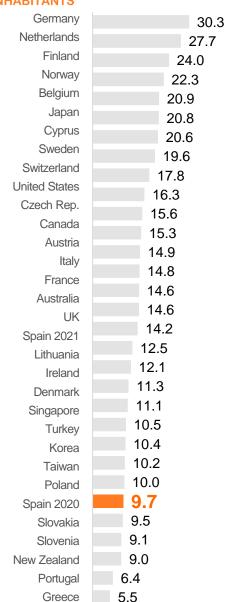




Situation at the end of 2020

Every year the World Marrow Donor Association (WMDA), the international association of registries, reports the global activity in the previous year. In 2020, a total of 22,361 transplants were performed around the world and 22,215 donations were processed. Spain is the **12**th **leading country in the world** and **5**th **in Europe** in terms of supplying haematopoietic progenitor cells for transplant.

TRANSPLANTS OF HAEMATOPOIETIC PROGENITOR CELLS FROM UNRELATED DONORS IN 2020 PER MILLION INHABITANTS



HAEMATOPOIETIC PROGENITOR CELL DONATIONS IN THE WORLD IN 2020*



^{*} Countries with fewer than 50 donations/year are not shown. The data refers to donations of haematopoietic progenitor cells from bone marrow, peripheral blood and umbilical cord blood.



^{*} Countries with fewer than 5 transplants/million inhabitants per year are not shown.









Donors

In 2021, the pandemic continued to have an impact on the registry's activity, with the following key points:

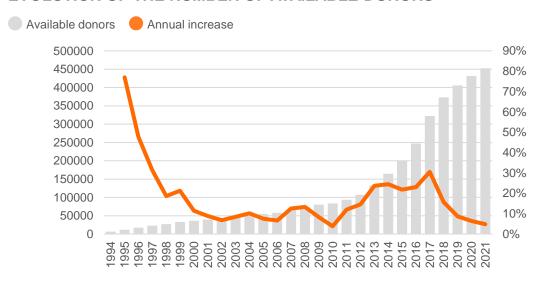
- We recorded a 5% increase in the number of available donors (*n*=452,552), which was higher than the worldwide average growth of 3%. However, the pandemic has had a very negative impact on donor recruitment over the last 2 years. The objective of the National Bone Marrow Plan is to reach the figure of 500,000 available donors. To achieve this, it is working on a national campaign to recruit new donors.
- REDMO now oversees donors residing in Andorra thanks to the agreements signed between the Government of Andorra, the National Transplant Organization and the Catalan Blood and Tissue Bank.
- The number of blood sample requests (a step prior to requesting a donation of haematopoietic progenitor cells) increased by 20% compared to the previous year, thanks to a rise in the number of donors, the drop in the average age of newly registered donors and the quality of the information (full HLA typing) that we have on them. Since the National Bone Marrow Plan was launched in 2012, growth has been continuous and has reached 180%.





452,552* Available donors in REDMO 5% rise in 2021

EVOLUTION OF THE NUMBER OF AVAILABLE DONORS

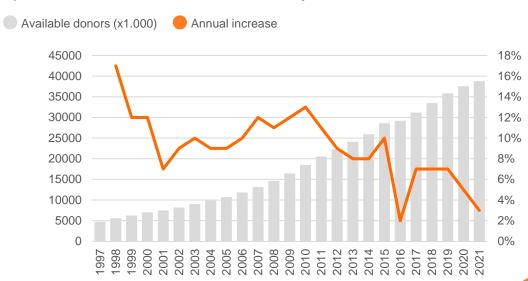


*The number of donors registered in REDMO may not match the number of donors reported by the National Transplant Organization or the Autonomous Regional transplant coordinators. REDMO only considers donors to be valid if they have completed all their basic details and their HLA typing. In contrast, the National Transplant Organization and the Autonomous Communities consider anybody who has given their informed consent and a sample for typing to be a donor.

38,787,508 Available donors in the world 3% rise in 2021

EVOLUTION OF AVAILABLE DONORS IN THE WORLD (×1.000)

Spain ranks 14th in the world and 7th in Europe.







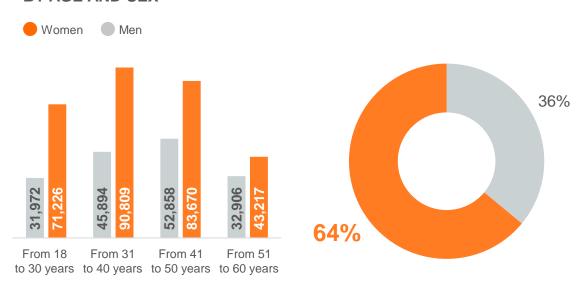




DONOR PROFILE

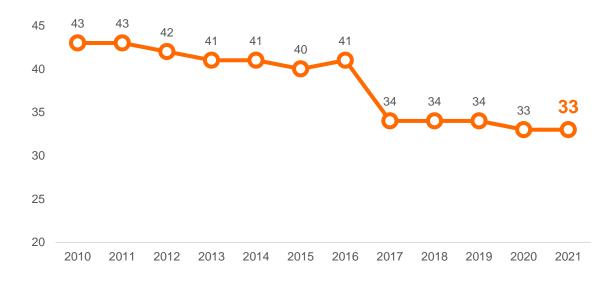
Profile of the available donors

BY AGE AND SEX



The average age of the available donors is **33 years old** (Standard deviation (SD) ± 10.2). **53%** of the available donors are **under 40 years old**, of whom only 36% are men.

EVOLUTION OF THE AVERAGE AGE OF AVAILABLE DONORS









DONOR PROFILE

Typing available donors

All our body's cells have molecules stuck to their surface known as HLAs (human leukocyte antigens).

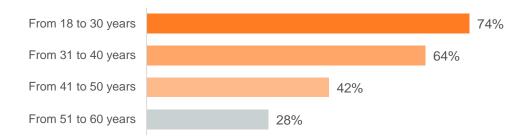
If two individuals share the same type of HLA, the patient's body will not consider the cells to be an alien body and will not reject them.

The HLA system is the main cause of the body rejecting grafts when there is insufficient compatibility between a patient and a donor.

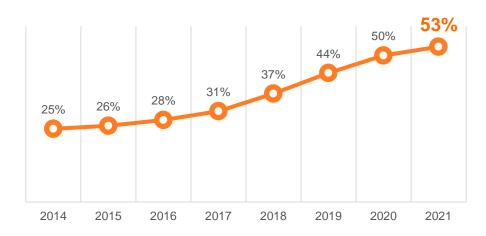
Good HLA typing of each donor enables us to select the most compatible donor for each patient faster and more efficiently. Between 2014 and 2021, we more than doubled the number of fully-typed donors thanks to:

- The incorporation of new technological tools in our laboratories (NGS)
- Initiatives to improve this indicator in collaboration with donor centres.

ACTIVE DONORS WITH FULL HLA TYPING* BY AGE GROUP



EVOLUTION OF THE PERCENTAGE OF ACTIVE DONORS WITH FULL HLA TYPING* (*n* = 452,552)





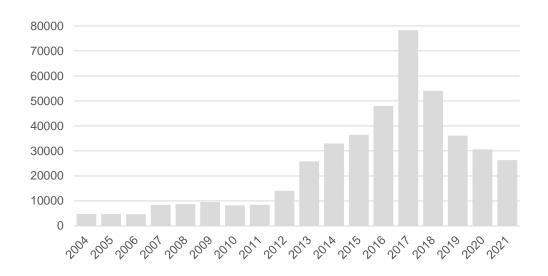
^{*} Full typing: HLA A, B, C and DRB1 (or HLA A, B, C, DRB1, DQB1 and DPB1).



Incorporation of new donors in REDMO

26,348 Donors incorporated in 2021 14% drop in 2021

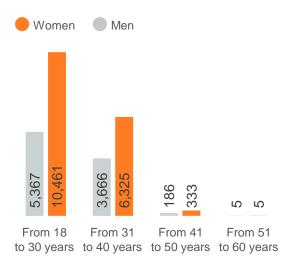
EVOLUTION OF THE ANNUAL INCORPORATION OF NEW DONORS

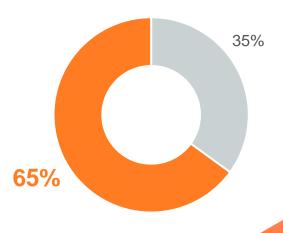


PROFILE OF DONORS INCORPORATED IN 2021 (n = 26.348)

The average age of the new donors is 29 years old (Standard deviation (SD) ±6.8).

98% of the new donors are **under 40 years old**, of whom only 35% are men.











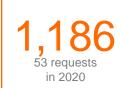
When a donor does not have a complete typing (A, B, C, DRB1 and DQB1), the transplant centre would request that the typing be extended from the donor's preserved sample at the time of registration.

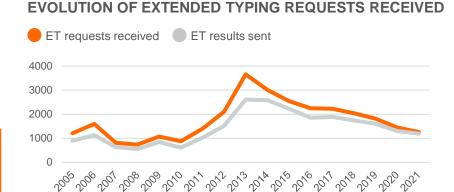
The number of ET requests has decreased by 15% compared to 2020 and by 190% since 2013 as a result of the increase in available donors with a complete typing.

Requests received



Results sent





Requests for blood sample for confirmatory typing (CT) in 2021

In order to verify that the typing performed on the donor is correct and compatible with the patient, the transplant center must perform a new complete typing of the donor from a new blood sample. The number of CT requests has increased by 20% compared to 2021 and by 186% since 2013, as a result of the increase in available donors with complete typing.

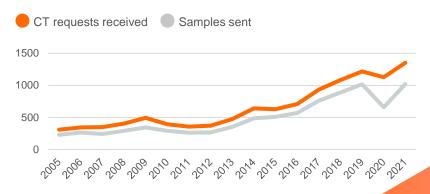
Requests received

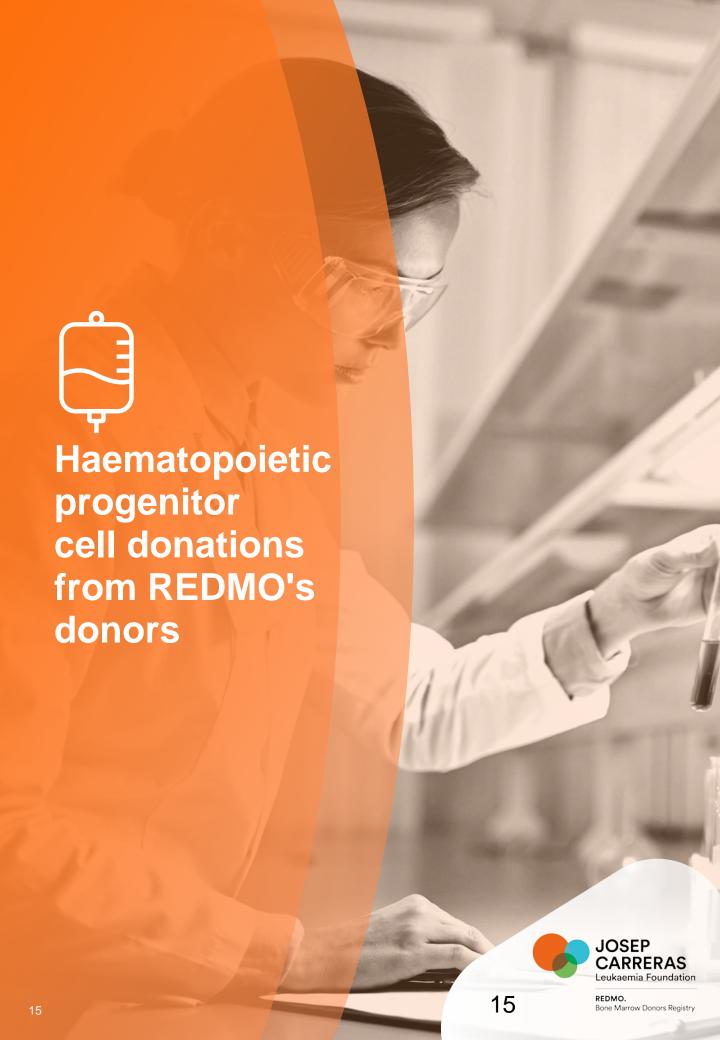


Samples processed

1,021
34 peticiones de 2020

EVOLUTION OF CONFIRMATORY TYPING SAMPLE REQUESTS RECEIVED











Haematopoietic progenitor cell donations from REDMO's donors

In 2021, we coordinated the donation of haematopoietic progenitor cells from 276 donors, which is a 25% increase with respect to 2020.

This was possible thanks to the increase in the number of donors and in the information available on them.

Most of the donors selected for transplant are young men. Therefore, the ratio of effective donations to available donors is currently 1 to 952 in the case of male donors and 1 to 2,779 in the case of the women available on the registry.

Moreover, the availability of our donors at the time of collection is 91%, which is very close to the target of 94% currently set by the World Marrow Donor Association (WMDA).

As a result of the annual growth in effective donations since the rollout of the National Bone Marrow Plan, the Autonomous Regional coordination teams, collection centres, the National Transplant Organization and REDMO have developed a new project that aims to standardize the donation process in order to improve the donors' experience and, at the same time, provide a more effective response to the growing demands of transplant centres all over the world.







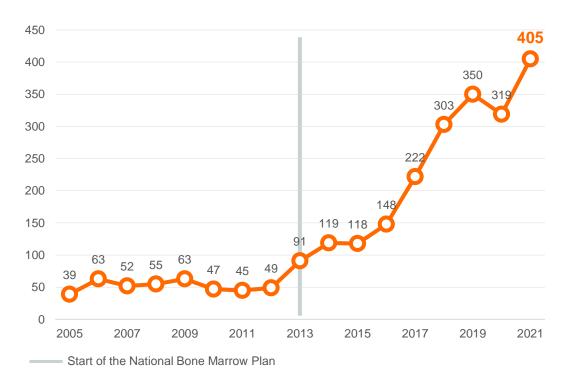
Donation requests in 2021

In 2021, we received an average of 8 donation requests per week and a new record was set in March, when we received 48. Donation requests **increased by 27%** compared to 2020.

Requests received	Effective donations	Collections in progress on 31/12/2021	Stopped before extraction
405 48 % international; 52 % national	276 15 requests in 2020	31	× 119*

^{*} Including postponed processes and 6 requests in 2020.

EVOLUTION OF DONATION REQUESTS BY YEAR





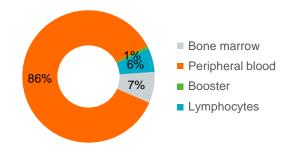
Donations coordinated in 2021

Effective donations

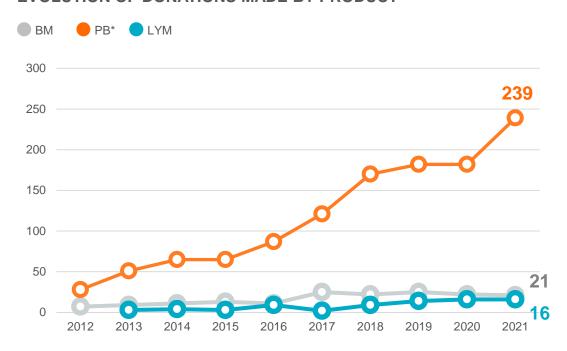
⊘	
276	
15 requests in 2020	

According to requested product	2021	2020
Bone marrow (BM)	21	20
Peripheral blood (PB)	237	179
CD34+ booster*	2	3
Lymphocytes (LYM)	16	16
Total	276	220

In 2021, an average of 5 donations per week were made. On 22/3/21, 8 donations were made in a single day, setting a new record for REDMO. Donations **increased by 25%** with respect to 2020.



EVOLUTION OF DONATIONS MADE BY PRODUCT



^{*} Booster CD34+: dose of stem cells

^{*} Includes 2 CD34+ boosters

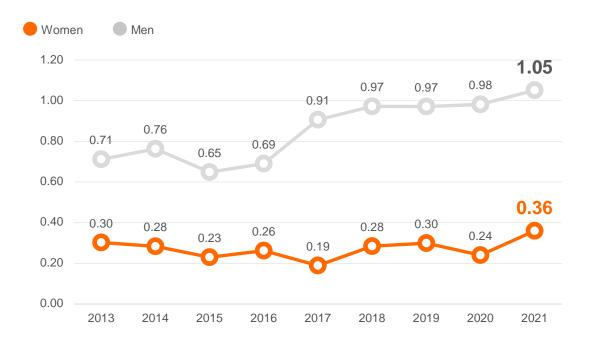


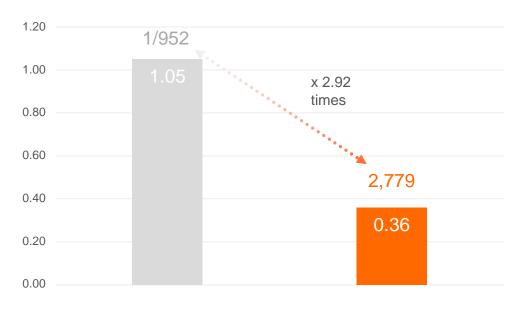
DISTRIBUTION OF DONATIONS BY EXTRACTION CENTRE AND PRODUCT (n=276)

Extraction Centre	BM (n = 21)	PBSC* (<i>n</i> = 239)	LYM (n = 16)	Total (<i>n</i> = 276)	Total CA
F. Jiménez Díaz	3	4		7	
H. 12 de Octubre		11	1	12	
H. Princesa	3	5		8	
H. Gregorio Marañón	1	7	2	10	66
H. La Paz		10	1	11	
H. Puerta de Hierro		10		10	
H. Ramón y Cajal	2	4	2	8	
Banc de Sang i Teixits		50	5	55	59
H. Clínic Barcelona	4			4	39
H. Carlos Haya	1	7		8	
H. de Jerez		4		4	
H. Reina Sofía	1	4		5	46
H. Virgen de las Nieves		10	2	12	
H. Virgen del Rocío		17		17	
H. Clínico de Valencia		8	1	9	20
H. La Fe	2	9		11	20
H. Morales Messeguer		12		12	20
H. Virgen de la Arrixaca		8		8	20
H. De Donostia	3	13		16	16
H. Miguel Servet		9		9	9
CHU de A Coruña		3	1	4	
CHU de Santiago de Compostela		4		4	9
CHU de Vigo		1		1	
H. Doctor Negrín		8		8	8
H. Clínico de Salamanca	1	6		7	7
H. Central Asturias		6		6	6
H. Marqués de Valdecilla		4	1	5	5
H. de Navarra		3		3	3
H. Son Espases		2		2	2



EVOLUTION OF THE RATIO OF DONATIONS PER 1,000 DONORS BY SEX





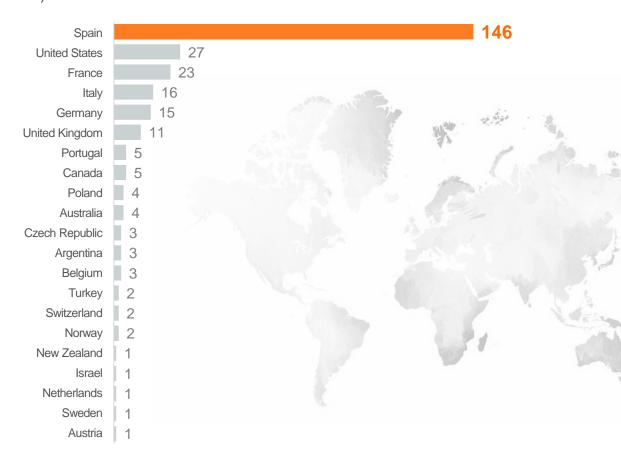
These graphs show that transplant centres preferentially request male donors for an effective donation of haematopoietic progenitor cells.



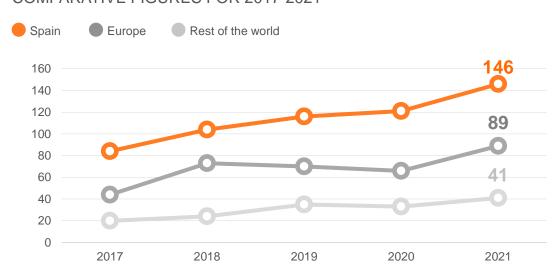




DISTRIBUTION OF DONATIONS BY DESTINATION COUNTRY (*n* = 276)



EVOLUTION OF EFFECTIVE DONATIONS BY DESTINATIONSCOMPARATIVE FIGURES FOR 2017-2021









Donor availability at the time of donation

The World Marrow Donor Association (WMDA) sets a target for all registries.

This indicator makes reference to the cencellation of **Bone Marrow or PB**

collection requests due to reasons related with the donor.

The target value defines that 94% of donors, or more, must be available.

BM/PB collection requests received



Collections cancelled for reasons related to the donor



91 %

Percentage of available donors

Reasons for cancelling collections	
Medical reasons	14
Donor or CC logistics	10
Voluntary withdrawal	9
Rejecting the product	2
Transferred to another registry	1





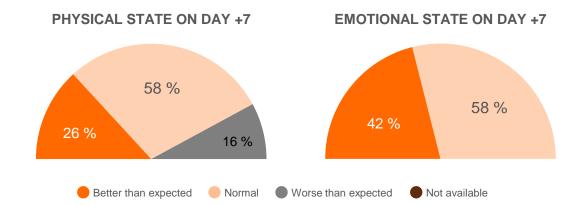


FOLLOW-UP 24 HOURS AND 7 DAYS AFTER THE DONATION OF BONE MARROW

In accordance with national and international regulations, registries must monitor the donor's physical and emotional state after the effective donation to ensure that they are not suffering from any negative effects as a result of the donation.







70% of donors presented some symptom during the 24-36 hours after donating bone marrow. The most common complaints detected are tiredness (25%) and pain at the puncture site (40%). A visit and assessment by the collection centre was only needed in one case.

Most symptoms disappeared within 7 days and 89% of donors have resumed their normal working routine and 79% of their usual physical activity.







FOLLOW-UP 24 HOURS AND 7 DAYS AFTER THE DONATION OF PERIPHERAL BLOOD

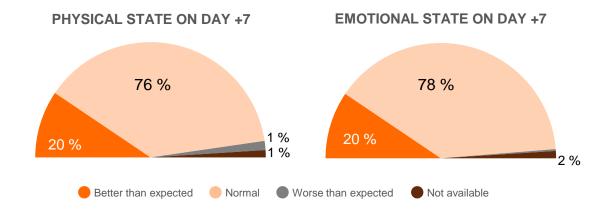
55% of donors presented some symptom during the 24-36 hours after donating peripheral blood. However, a visit and assessment by the collection centre was only needed in six cases. The most common complaints detected are tiredness (24%) and bone and muscle pain (34%). Most symptoms disappeared within 7 days and 99% of donors have resumed their normal working routine and 95% of their usual physical activity.



Effective



Follow-ups











Umbilical Cord Blood (UCB) Units

In the case of umbilical cord blood, the National Umbilical Cord Blood Donation Plan (NUCBDP) drafted in 2008 sets out guidelines for the banks' activities and their expected growth. The first UCB started to be stored in 1997 (n=485) and has since climbed to the current total of 64,109.

The NUCBDP stipulates that the optimal number of stored UCB units was 60,000 to be able to offer the possibility of a transplant to all the patients who needed one, considering the compatibility required between the patient and the cord is not as high as in the case of an adult donor. Moreover, the NUCBDP established the minimum criteria for cryopreserving units.

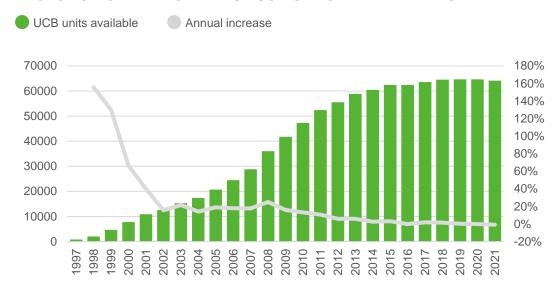
Spain has always been a global leader in terms of cord blood units, ranking in the top 5 in the world and the top 3 in Europe.

The evolution of UCB units shipment has been different from all other REDMO activities due to the arrival of new therapies for patients, which have meant that in recent years this type of transplants has decreased, therefore, the number of shipments has also been reduced.





EVOLUTION OF THE NUMBER OF UCB UNITS AVAILABLE IN SPAIN

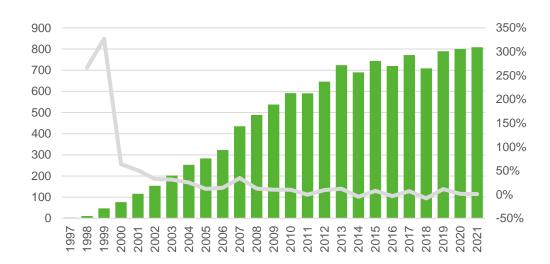


64,109 UCB units available in Spain

236 Incorporations in 2021

EVOLUTION OF UCB UNITS AVAILABLE IN THE WORLD (×1.000)





809,374 Cord Blood Units available in the world Increase 2021: 1 %









Extended Typing (ET) requests in 2021

90 Requests received

77 Results sent

9 Days average response time

EVOLUTION OF EXTENDED TYPING (ET) REQUESTS



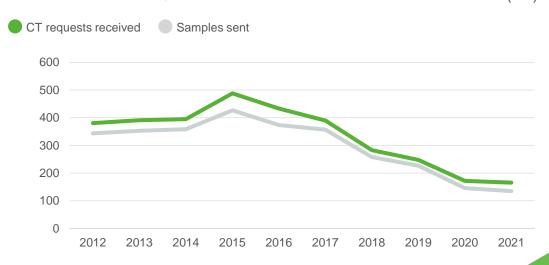
DNA samples (CT) requests in 2021

166 Requests received 3 % drop

135 Samples sent

6 Days average response time

EVOLUTION OF REQUESTS FOR CONFIRMATORY DNA SAMPLE (CT)









Requests to reserve UCB units in 2021

116 Requests received 24% drop

89 Final reports

1 Days average response time

EVOLUTION OF RESERVE REQUESTS



Reserving an umbilical cord blood unit is a step prior to shipment of a unit for transplant. The Cord Blood Bank firstly reviews and expands the information on the unit in order to verify that it is optimal for its subsequent transplant.

To do so, it checks the HLA typing, blood group, infectious disease markers of the mother and the child, the child's state of health, and the expected behavior of the unit once transplanted to the patient.







Shipments of units of UCB in 2021

Requests received

129
92 % international;
8 % national

UCB units shipped

109 2 requests in 2020 Shipments cancelled

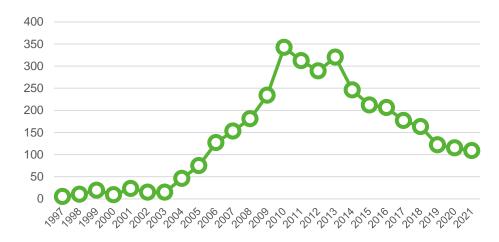
× 16 Shipments in progress

6 on 31/12/2021

EVOLUTION OF SHIPMENTS OF UCB UNITS



EVOLUTION OF SHIPMENTS MADE BY DESTINATION



109 Shipments in 2021 5 % drop





UCB SHIPMENT DISTRIBUTION BY COUNTRY OF DESTINATION.

Total 2019-2021

United Kingdom

Canada

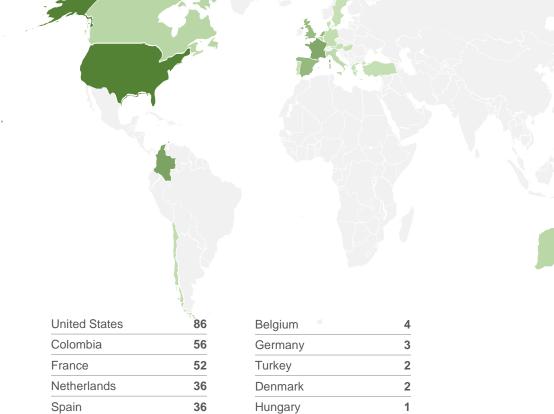
Australia

Italy Chile 34

10

9

Over the last three years, REDMO has coordinated the shipment of **346 Umbilical Cord Blood Units** for patients all over the world.



Germany	3
Turkey	2
Denmark	2
Hungary	1
Portugal	1
Greece	1
Sweden	1
New Zealand	1
Austria	1









Patients

The processes coordinated by REDMO for national patients that require a transplant from an unrelated donor have undergone the biggest changes of any of our processes over the years.

Initially, the number of available donors and technically shortcomings meant that search times to find a compatible donor were extremely long.

The process originally took over 100 days to locate a suitable donor for a transplant. Nowadays, a search takes an average of 26 days. This reduction in the search time has enabled us to give an opportunity a patients for whom time is a critical factor and who cannot wait several weeks to receive a transplant.

Although the number of patients for whom new search requests for an unrelated donor are initited remains stable (just a 2% rise in patients starting a search), the number of donors located for these patients has risen

by10%, which represents a significant improvement in the efficiency of the search process.

Before last year, we had never surpassed the threshold of 500 transplants in a year but, in 2021, we managed to perform a total of 600 (583 from bone marrow or peripheral blood and 17 from cord blood), which equates to over 11 donations per week for our patients.



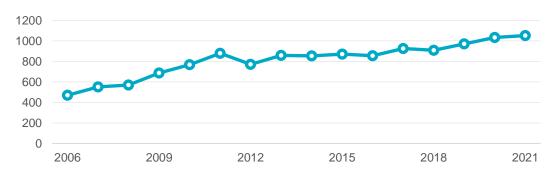


1,053 Searches activated 2% rise in 2021

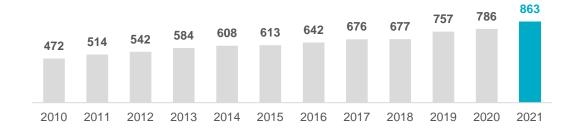
Since 2006, we have initiated searches for over 13,000 patients. Last year, we started around 3 searches per day.

In 2021, we initiated 1,053 searches for unrelated donors for Spanish patients. Moreover, for 863 patients, we located at least 1 available and compatible donor.

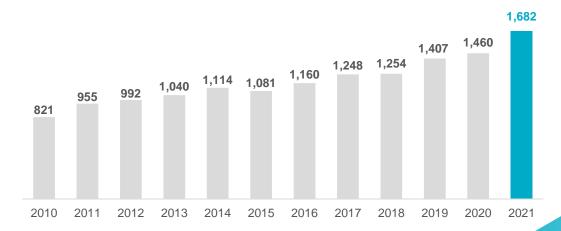
EVOLUTION OF SEARCH ACTIVATIONS



Patients with a donor located



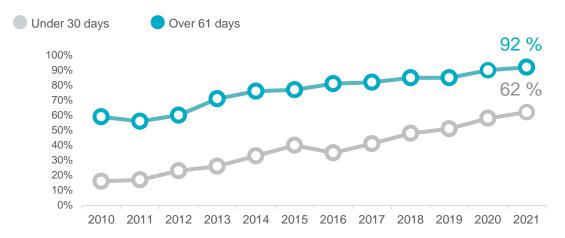
1,696 Donors located







DONOR LOCATION TIME

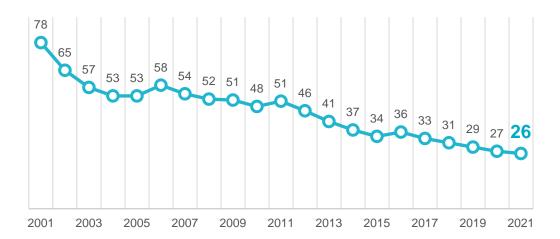


BM/PB donor location time (n = 863)	
Under 30 days	(62 %) 535
Between 31 and 61 days	(30 %) 260
Between 62 and 90 days	40
Over 3 months	15
Over 6 months	13

92% Donors located in under 2 months

62% Donors located in under 30 days

26 Days average response time

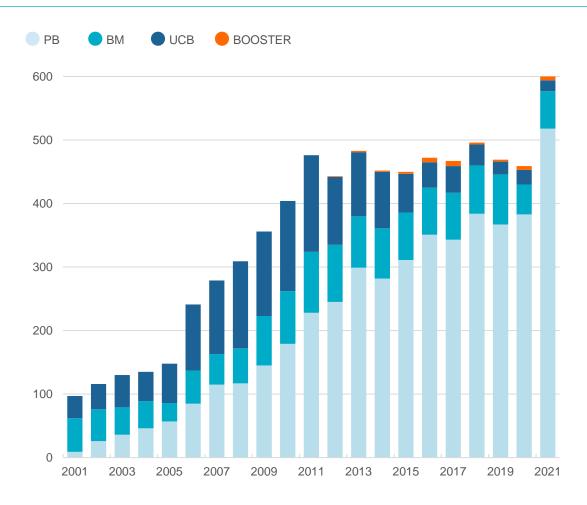








600 Unrelated donor haematopoietic transplants 2021 31% rise in 2021



PB = Peripheral blood (*n*=518)

BM = Bone marrow (n=59)

UCB = Umbilical cord blood (*n*=17)

BOOSTER = Stem cells booster dose (*n*=6)







DISTRIBUTION OF TRANSPLANTS BY TRANSPLANT CENTER AND PRODUCT (n = 600)

	B mar	one row		heral lood*	UCB	Total transplants	Total
Hospital	<=15 years	>15	<=15	>15	<=15 >15	per hospital (2020)	community (2020)
H. Carlos Haya – Unidad pediátrica	3	years	1	years	years years	4 (4)	(2020)
H. Carlos Haya – Unidad adultos		2		17		19 (23)	
H. de Jerez				12		12 (10)	
H. Reina Sofía	1	1		4		6 (1)	108 (82)
H. Virgen de las Nieves		1		21		22 (16)	
H. Virgen del Rocío – Unidad pediátrica	1	•	1	1	2	5 (8)	
H. Virgen del Rocío – Unidad adultos		2		38		40 (19)	
H. Central de Asturias		1	1	15		17 (12)	17 (12)
H. Son Espases		2		12		14 (9)	14 (9)
H. Dr. Negrín				14		14 (6)	14 (6)
H. Marqués de Valdecilla	1	4		19		24 (19)	24 (19)
H. Clínico de Salamanca	'	1	3	21		25 (16)	25 (16)
CS Vall d'Hebron – Unidad pediátrica	8	1	5	3	4	21 (16)	23 (10)
CS Vall d'Hebron – Unidad adultos	0		- 0	29		29 (14)	
H. Clínic i Provincial		1		31		32 (28)	
H. de Sant Pau – Unidad pediátrica	1		1	31		2 (2)	
H. de Sant Pau – Unidad adultos	'	3	'	21		24 (27)	153 (122)
H. Sant Joan de Déu	3	3	4	2	2	11 (7)	
H. Germans Trias i Pujol	3		-	12		12 (15)	
H. Duran i Reynals				22		22 (13)	
H. Ramon y Cajal				8		8 (1)	
H. de la Princesa		1		13		14 (11)	
H. Gregorio Marañón – Unidad pediátrica	2			10		2 (1)	
H. Gregorio Marañón – Unidad adultos		1		11		12 (4)	
H. La Paz – Unidad pediátrica	4		5	3	1	13 (8)	
H. La Paz – Unidad adultos		1		3	'	4 (5)	88 (62)
H. 12 de Octubre				7		7 (5)	
H. Niño Jesús	3	1	5	3	2	14 (13)	
H. Univ. Puerta de Hierro		1	- 0	1	3		
H. Morales Messeguer		•		1		1 (3)	
H. Virgen de la Arrixaca	2		2	4		8 (2)	9 (5)
H. Clínic Valencia – Unidad pediátrica	1			7		1 (0)	
H. Clínico Valencia – Unidad adultos	- 1			20		20 (11)	60 (53)
H. La Fe - Unidad pediátrica	2		2	1		5 (16)	00 (33)
H. La Fe - Unidad adultos		2		30	2		
CHU de A Coruña				9		9 (9)	
CHU de Santiago – Unidad pediátrica			1	1		2 (4)	
CHU de Santiago – Unidad adultos			'	22		22 (10)	41 (33)
CHU de Vigo				8		8 (10)	
H. de Navarra				12		12 (7)	
Clínica de Navarra			1	4	1	6 (3)	18 (10)
H. Donostia	1		1	28	'	29 (30)	29 (30)
Total		26	32	492	12 5		600 (459)



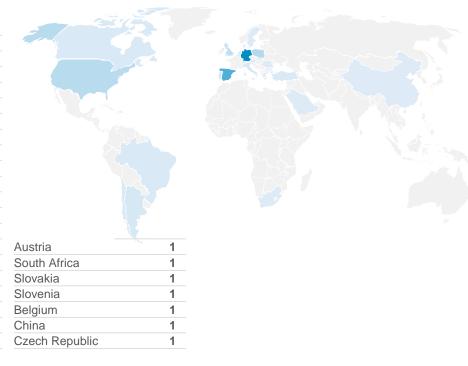
583 BM/PB* transplants in 2021

17 UCB transplants in 2021

* Including 6 CD34+ boosters

BY COUNTRY OF ORIGIN OF THE BM/PB

Germany	(37 %) 216
Spain	(24 %) 139
Poland	41
United States	37
United Kingdom	32
Israel	29
Netherlands	11
Portugal	11
Italy	9
Argentina	8
Chile	6
Brazil	6
Canada	6
Turkey	5
Switzerland	5
Cyprus	3
Denmark	2
Greece	2
Sweden	1
Romania	1
Saudi Arabia	1



BY COUNTRY OF ORIGIN OF THE UCB (n = 17)

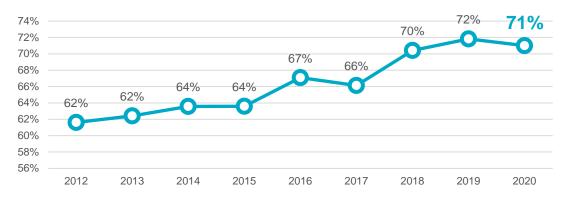
Spain	11
United States	4
France	1
Italy	1





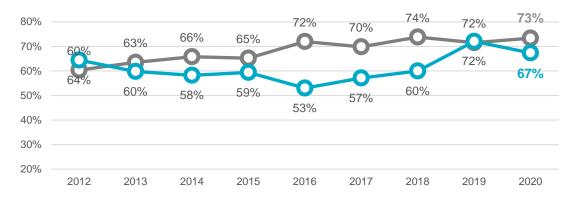


SURVIVAL RATE 1 YEAR AFTER BM/PB TRANSPLANT IN MALIGNANT DISEASES (n = 3,238)



SURVIVAL RATE 1 YEAR AFTER BM/PB TRANSPLANT IN MALIGNANT DISEASES BY COMPATIBILITY (n = 3,233*)





^{* 5} patients transplanted from donors with lower compatibility.

FOLLOW-UP 1 YEAR AFTER DONATION FROM A RELATED DONOR

3,810 Collections 2012-2020

2nd collections for the same patient (n = 240) (BM=11; PB=61; LYM=132; CD34+ booster=36)

3,570 1st tran

1st transplant

Malignant diseases 3,238**

Non-malignant diseases* 332



^{*}Non-malignant diseases: bone marrow aplasia, congenital erythrocytic diseases, congenital immune system diseases, congenital metabolic diseases and other non-malignant diseases.

^{** 6} patients with no information as follow-up missed at the transplant centre.





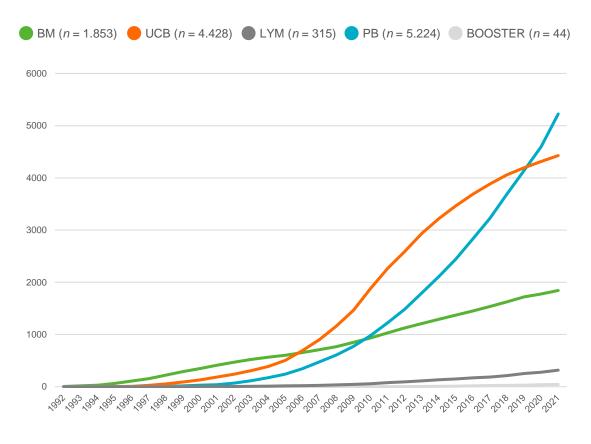
REDMO's global activity 1991-2021

PROCEDURES COORDINATED BY REDMO

DONORSBM / PB / BOOSTER / UCB / LYM

P	ΙF	N	TS	

	Spanish	Foreign	Total
Spanish	1,758	6,408	8,166
Foreign	3,688		3,688
Total	5,446	6,408	11,854



BM = Bone marrow

BOOSTER = Peripheral blood (stem cell booster)

PB = Peripheral blood

LYM = Lymphocytes



REDMO.

Bone Marrow Donors Registry

C/ Muntaner, 383, 2-2 08021 Barcelona Phone. 93 414 55 66 I Fax. 93 414 00 28 redmo@fcarreras.es

www.fcarreras.org