TRANSFUSION MEDICINE

BLOODchip ID

Efficient blood group genotyping for extended matching

TYPING

GRIFOLS

BLOOD chip ID

The same commitment as the first day

At Grifols, we know the primary concern in blood transfusion is patient safety. With 75 years of experience in the field of transfusion medicine, safety is also our number one priority.

Blood Group Genotyping (BGG) takes safety a step further. Progenika Biopharma, a Grifols company, launched its first BGG product in 2007[1]. During these 10 years, our products have been used worldwide to extensively type donors and patients, with excellent performance[2].

75 YEARS of experience in transfusion medicine

10 YEARS of BGG product availability

1. *Product registration and availability vary by country. To know whether a product is available in your country, please kindly contact your Grifols representative.* ***2.*** *Finning et al. Blood Transfus. 2016 Mar;14(2):160-7, 2 (This study was supported by Grifols)*

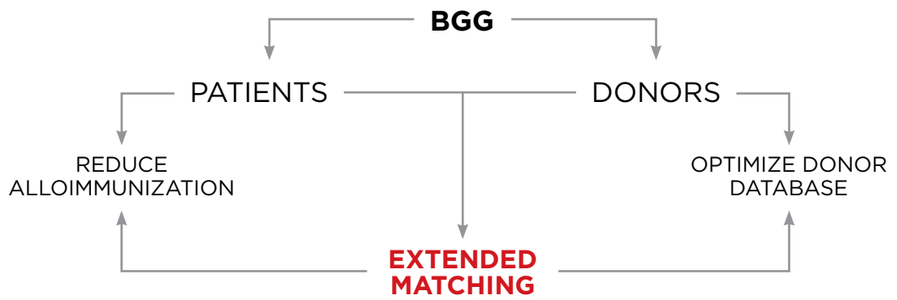
Genotyping: when and why?

Molecular typing has been proven very effective in overcoming some well-known serology limitations such as[1]:

- Typing recently and chronically transfused patients
- DAT positive samples
- Weak expressions
- When antisera is not available

Main applications and benefits of BGG

	CLINICAL SITUATION	BENEFITS
PATIENTS	• Chronically transfused patients (SCD, thalassemia, cancer patients) • Autoimmune hemolytic anemia • Pregnancy • Patients under monoclonal treatments such as anti-CD38	• Prospective extended matching has been shown to reduce alloimmunization rates[2,3] • Reduction of alloimmunization rates is associated with: - Increased patient survival[4,5] - Expansion of period between transfusions[6]
DONORS	• When antisera is not available • To build extensively typed donor databases	• Reduction of costs to provide antigen negative units[7] • Save in reagent and labor cost[8] • Reduction of time to provide antigen negative units[7] • Better management of negative units stocks (ie, Duffy b and D neg)[9,10,11]



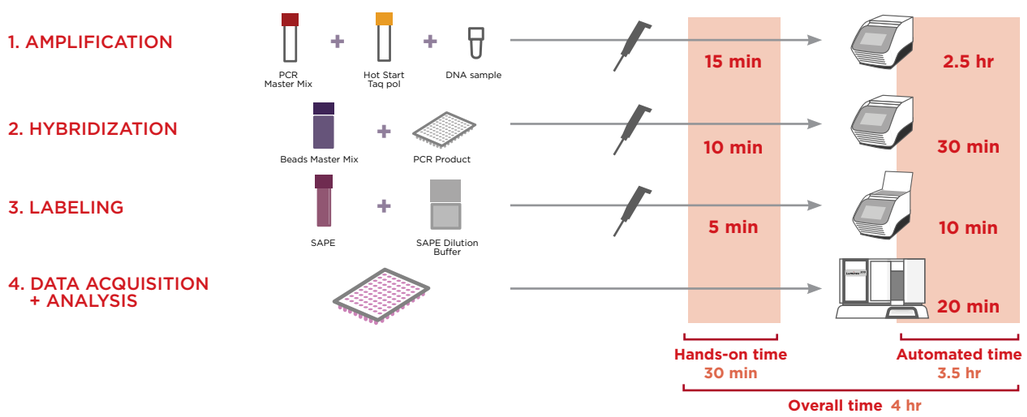
1. *Jungbauer, ISBT Science Series (2011) 6, 399-403;* ***2.*** *Lasalle-Williams et al. Transfusion. 2011 Aug;51(8):1732-9.* ***3.*** *Tahhan et al, Transfusion. 1994 Jul;34(7):562-9.* ***4.*** *Telen et al. Transfusion. 2015 Jun;55(6 Pt 2):1378-87;* ***5.*** *Nickel et al. Transfusion. 2016 Jan;56(1):107-14.* ***6.*** *Da Costa DC et al. Rev Bras Hematol Hemoter. 2013;35(1):35-8.* ***7.*** *Shafi et al, Transfusion. 2014 May;54(5):1212-9;* ***8.*** *Winkler et al, Immunohematology. 2012;28(1):24-6.* ***9.*** *Sandler et al Transfusion. 2015 Mar;55(3):680-9.* ***10.*** *Flegel, Transfus Apher Sci. 2011 Feb;44(1):81-91.* ***11.*** *Peiper et al. J Exp Med. 1995 Apr 1;181(4):1311-7*

BLOODchip ID

Easy and fast process

FEATURES		BENEFITS
EASY	• Only 4 tubes to pipette • No washing steps • Ready-to-use reagents	• Easy for technicians of all levels • Reduces human errors
FAST	• 4 hr from DNA to results[1,2] • 30 min hands-on time[1,2]	• Results are obtained quickly • Technicians are available to perform other activities
FLEXIBLE	• 1-96 tests per run • Multiple-batch: ID CORE XT, ID HPA XT, and ID RHD XT can be performed in the same run • Open technology: standard Luminex® equipment can be used for other products	• Results obtained when needed, without running full batches • Different product results can be obtained simultaneously, which improves efficiency and reduces time and resources. • Efficient equipment investment

BLOODchip ID analytical procedure



Accurate and reliable performance

PARAMETER	RESULT	STUDY DESCRIPTION	REFERENCE
ACCURACY (SPECIFICITY AND SENSITIVITY)	**100%**	• Multi-center study: Milan (Italy), Barcelona (Spain), Bristol and Aberdeen (UK) • 519 samples compared with reference methods	• Finning et al. Blood Transfus. 2016 Mar;14(2):160-7, 2 (This study was supported by Grifols)
	100%	• Study performed in Brazil. 242 samples compared with Open Array and with sequencing if discrepant results	• Bianchi et al, ISBT Science Series Volume 10, Issue 1, pages 45–51 (Grifols company supplied the inputs for the assays ID CORE XT and ID HPA XT)
	100%	• 1000 samples tested at 2 sites were compared with CE marked serology assays following Directive 98/79/CE. Antigens were compared with molecular reference methods when serology wasn't available.	• ID CORE XT package insert (pages 18-19)
	100%	• 283 samples tested at 1 site were compared with established molecular genotyping reference methods	• ID HPA XT package insert (pages 16-17)
	100%	• 1000 samples were processed with ID RHD XT following Directive 98/79/CE. Results were compared with RHD serology in every case and with bidirectional sequencing in the case of Weak D samples (n=163). Discrepancies were resolved with bi – directional sequencing	• ID CORE XT package insert (pages 18-19)
r'S ACCURACY	**99%**	• Study performed in US. 125 possible r'S samples were tested with HEA beadchip (Immucor) and with ID CORE XT. ID CORE XT could accurately detect r'S type 1 haplotype in one single test.	• Moulds et al. Transfusion. 2015 Jun;55(6 Pt 2):1418-22 (Joann M. Moulds and Katrina L. Billingsley were consultants for Novartis and Grifols)
PRECISION	**100%**	• Use of the analytical procedure in different laboratories, and use of analytical procedure on different days, with different operators and different equipment within the same laboratory.	• ID CORE XT (pages 18-19) and ID HPA XT (page 17) package inserts

1. *Finning et al. Blood Transfus. 2016 Mar;14(2):160-7, 2 (This study was supported by Grifols).*
2. *ID CORE XT package insert, page 10.*

ID CORE XT

- **Analyzes 29 polymorphisms determining 37 RBC antigens**
- **48 tests per kit**

Main applications[1,2]

- Assess the presence/absence of blood groups in chronically transfused patients
- Screen routine donors
- Select compatible donors for alloimmunized patients
- Complement serological panel with further antigen identification
- Type patients treated with drugs such as daratumumab, that interfere with blood typing methods

1. *Jungbauer, ISBT Science Series (2011) 6, 399-403*
2. *AABB Association Bulletin #16-02*

ID CORE XT antigen panel

BLOOD GROUPS	ALLELES ASSAYED	PHENOTYPES (ANTIGENS)
RHCE	*RHCE*CeCW; RHCE*ceCW* *RHCE*CECW; RHCE*ce; RHCE*cE;* *RHCE*Ce; RHCE*CE; RHCE*ceAR* *RHCE*ce[712G]; RHCE*CeFV* *RHCE*cEFM; RHCE*ce[733G]* *RHCE*ce[733G,1006T]* *RHCE*CeVG; RHCE*cE[712G,733G]* *RHCE*Ce[733G]; RHD*r's-* *RHCE*ce[733G,1006T]* *RHCE*CE-D[5, 7]-CE*	**C** (RH2) **E** (RH3) **c** (RH4) **e** (RH5) **CW** (RH8) **V** (RH10) **hrS** (RH19) **VS** (RH20) **hrB** (RH31)
KELL	*KEL*K_KPB_JSB; KEL*k_KPB_JSB* *KEL*k_KPA_JSB; KEL*k_KPB_JSA*	**K** (KEL1) **k** (KEL2) **Kpa** (KEL3) **Kpb** (KEL4) **Jsa** (KEL6) **Jsb** (KEL7)
KIDD	*JK*B_null(IVS5-1a)* *JK*A_null(IVS5-1a); JK*A; JK*B* *JK*B_null(871C)*	**Jka** (JK1) **Jkb** (JK2)
DUFFY	*FY*A_GATA; FY*B_GATA; FY*A FY*B* *FY*A[265T]* *FY*B[265T]_FY*X*	**Fya** (FY1) **Fyb** (FY2)
MNS	*GYPA*M; GYPA*N; GYPB*S; GYPB*s* *GYPB*S_null(230T)* *GYPB*S_null(IVS5+5t)* *GYP.Mur; GYPB*deletion*	**M** (MNS1) **N** (MNS2) **S** (MNS3) **s** (MNS4) **U** (MNS5) **Mia** (MNS7)
DIEGO	*DI*A; DI*B*	**Dia** (DI1) **Dib** (DI2)
DOMBROCK	*DO*A; DO*B; DO*B_HY* *DO*A_JO*	**Doa** (DO1) **Dob** (DO2) **Hy** (DO4) **Joa** (DO5)
COLTON	*CO*A; CO*B*	**Coa** (CO1) **Cob** (CO2)
CARTWRIGHT	*YT*A; YT*B*	**Yta** (YT1) **Ytb** (YT2)
LUTHERAN	*LU*A; LU*B*	**Lua** (LU1) **Lub** (LU2)

ID HPA XT

- **Analyzes 13 polymorphisms determining 12 HPA systems**
- **48 tests per kit**

Main applications[1]

- Platelet antigen typing in donors and patients
- Perform large-scale donor typing for provision of antigen-negative platelets
- Help to select compatible platelet donors for refractory or alloimmunized patients
- Complement clinical history of alloimmune platelet disorders, such as foetal and neonatal alloimmune thrombocytopenia (FNAIT), post-transfusion purpura, and platelet transfusion refractoriness

1. *Hurd et al. Vox Sanguinis (2002) 83, 1–12*

ID HPA XT antigen panel

HUMAN PLATELET ANTIGENS	ALLELES ASSAYED	PHENOTYPES (ANTIGENS)
HPA-1	*HPA1a; HPA1b*	HPA-1a; HPA-1b
HPA-2	*HPA2a; HPA2b*	HPA-2a; HPA-2b
HPA-3	*HPA3a; HPA3b*	HPA-3a; HPA-3b
HPA-4	*HPA4a; HPA4b*	HPA-4a; HPA-4b
HPA-5	*HPA5a; HPA5b*	HPA-5a; HPA-5b
HPA-6	*HPA6a; HPA6b*	HPA-6bw
HPA-7	*HPA7a; HPA7b*	HPA-7bw
HPA-8	*HPA8a; HPA8b*	HPA-8bw
HPA-9	*HPA9a; HPA9b*	HPA-9bw
HPA-10	*HPA10a; HPA10b*	HPA-10bw
HPA-11	*HPA11a; HPA11b*	HPA-11bw
HPA-15	*HPA15a; HPA15b*	HPA-15a; HPA-15b

IDRHD^XT

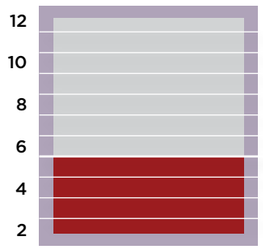
ID RHD XT

- **Analyzes 7 polymorphisms determining 6 RHD variants and HPA-1**
- **24 tests per kit**

Main applications[1,2]

- Weak D patient subtyping to rationalize the use of D neg blood units
- Weak D pregnant women subtyping to avoid unnecessary RhIG injections
- Confirmation of D neg donors

Blood stocks: O-



D neg units are scarce

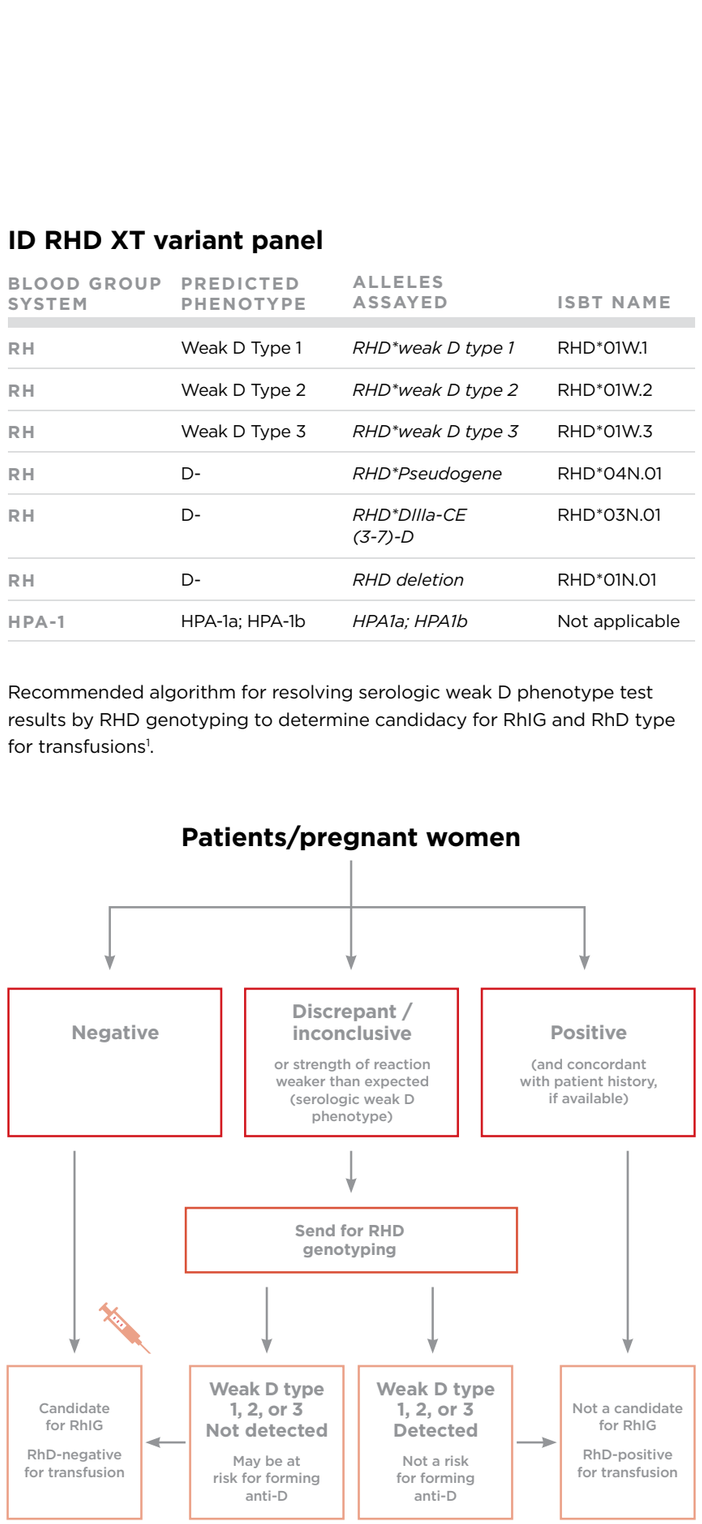
1. *Sandler et al Transfusion. 2015 Mar;55(3):680-9.*
2. *Lopez et al. Vox Sanguinis, Volume 111, Issue Supplement S1, Page 234*

ID RHD XT variant panel

BLOOD GROUP SYSTEM	PREDICTED PHENOTYPE	ALLELES ASSAYED	ISBT NAME
RH	Weak D Type 1	*RHD*weak D type 1*	RHD*01W.1
RH	Weak D Type 2	*RHD*weak D type 2*	RHD*01W.2
RH	Weak D Type 3	*RHD*weak D type 3*	RHD*01W.3
RH	D-	*RHD*Pseudogene*	RHD*04N.01
RH	D-	*RHD*DIIIa-CE (3-7)-D*	RHD*03N.01
RH	D-	*RHD deletion*	RHD*01N.01
HPA-1	HPA-1a; HPA-1b	*HPA1a; HPA1b*	Not applicable

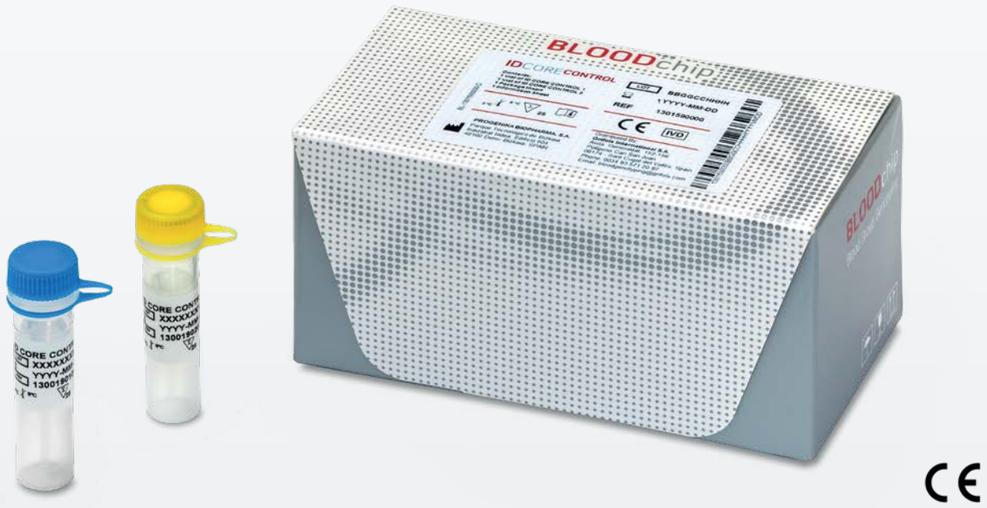
Recommended algorithm for resolving serologic weak D phenotype test results by RHD genotyping to determine candidacy for RhIG and RhD type for transfusions[1].

Patients/pregnant women



1. *Sandler et al Transfusion. 2015 Mar;55(3):680-9.*

IDCORECONTROL



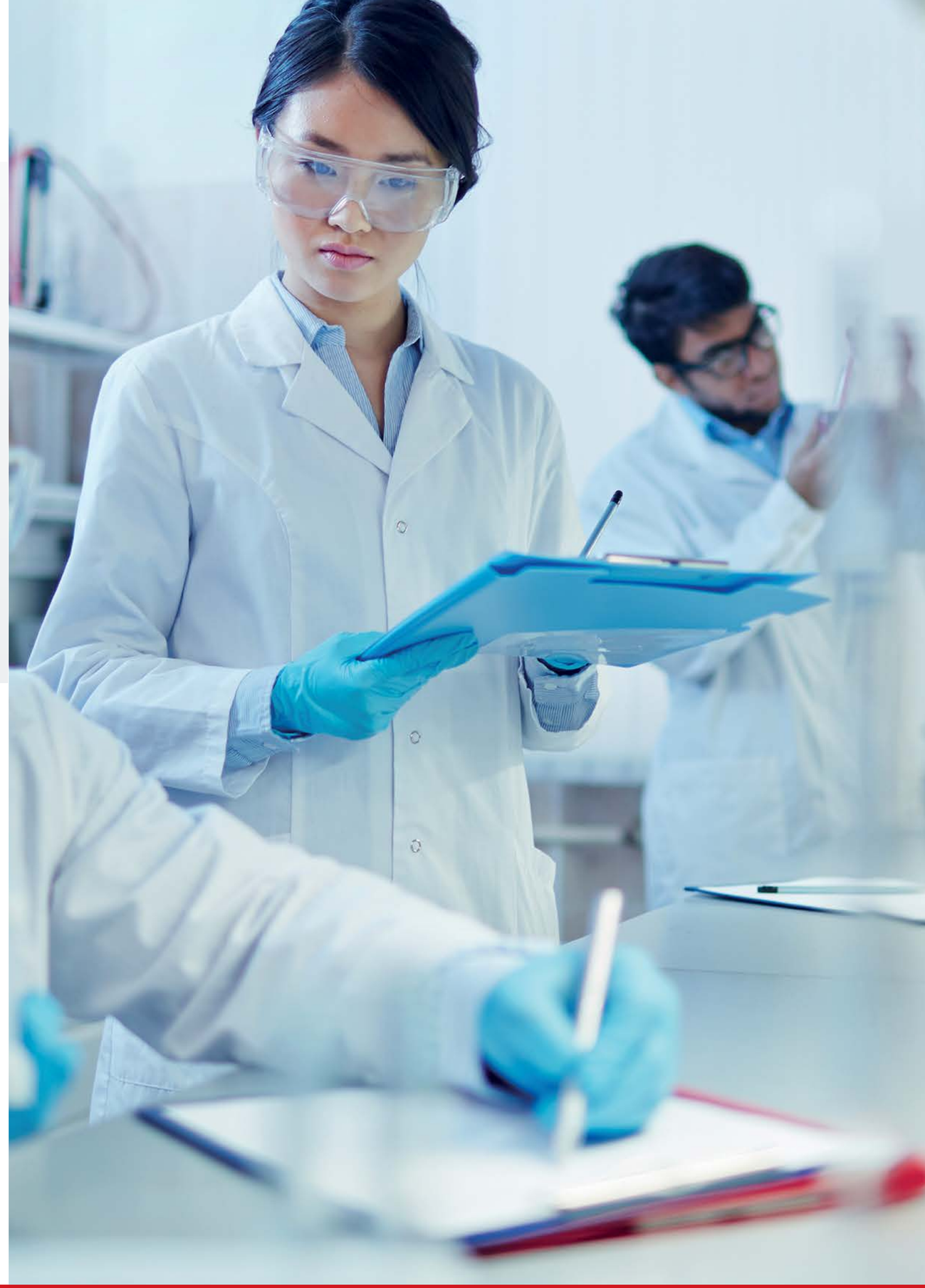
CE

ID CORE CONTROL is a positive control for ID CORE XT

- **2 clones including testing for all allele A and B of all polymorphisms tested in ID CORE XT**
- **25 tests per kit**

Main benefits

- Standardization of the system quality control processes
- Practical: already commercially available, the laboratory does not have to produce their own controls
- Allows control of all tested alleles



CE

BLOODchip ID software efficiently handles the genotyping procedure and data

Workflow traceability
- Plate configuration, kit and enzyme lot registration
- Worksheet print-outs with calculated volumes to pipette

Database and multiple-search function
- Comprehensive database for samples, clinical information, and test results
- Multiple-search function, including phenotypes and genotypes

Clear results
- Friendly and detailed reports
- Results by sample or batch of samples
- Multiple report formats (.xls, .pdf)
- Results are generated automatically, no user intervention for interpretation

Connectivity
- Connection with LIS
- Connection with Luminex

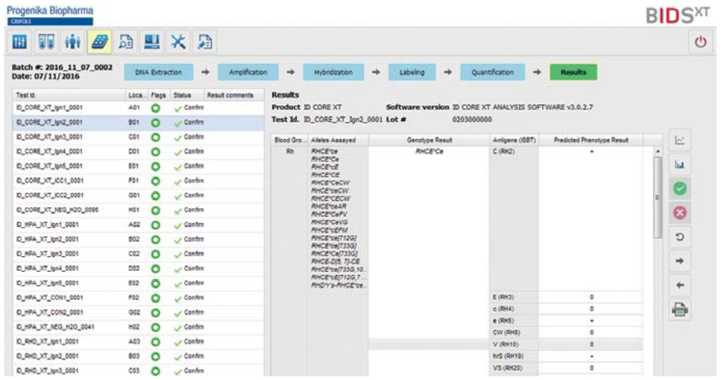
Performance and quality control
- Provides management of positive and negative controls
- Provides performance statistics
- Provides raw data graphs for troubleshooting

Audits
- Registers all actions performed by users

Configurable
Comprehensive
Flexible

BIDS XT results window

Assists the user throughout the analytical procedure. Results are automatically shown on screen following Luminex quantification.



BIDS XT worksheet

Provides printable worksheets, which include plate design, reagent lot numbers and automatic calculation of volumes to facilitate the process and avoid errors.

Batch #: 2016_11_07_0002
Comments:

AMPLIFICATION

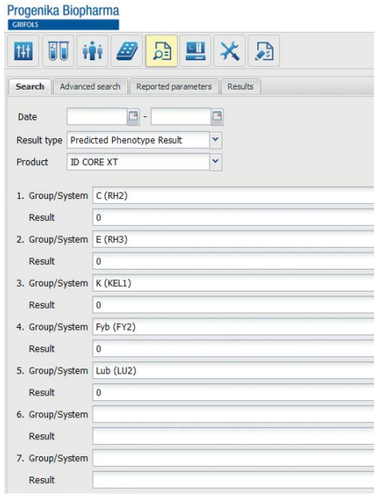
	1	2	3	4	5	6	7	8	9	10	11	12
A	Ign1 ID CORE XT	Ign1 ID HPA XT	Ign1 ID RHD XT									
B	Ign2 ID CORE XT	Ign2 ID HPA XT	Ign2 ID RHD XT									
C	Ign3 ID CORE XT	Ign3 ID HPA XT	Ign3 ID RHD XT									
D	Ign4 ID CORE XT	Ign4 ID HPA XT	Ign4 ID RHD XT									
E	Ign5 ID CORE XT	Ign5 ID HPA XT	Ign5 ID RHD XT									
F	ICC1 ID CORE XT	CON1 ID HPA XT	CON1 ID RHD XT									
G	ICC2 ID CORE XT	CON2 ID HPA XT	CON2 ID RHD XT									
H	H2O ID CORE XT	H2O ID HPA XT	H2O ID RHD XT									

PRODUCT	ID CORE XT		
Kit #	0203000000		
Tests #	8		
REAGENTS	**LOT #**	**Volume (µl)**	**Check**
ID CORE XT PCR Master Mix	0203000006	180.0	
HotStarTaq DNA Polymerase (5 U/µL)	HEA16-12A	4.0	

PRODUCT	ID HPA XT		
Kit #	0102000000		
Tests #	8		
REAGENTS	**LOT #**	**Volume (µl)**	**Check**
ID HPA XT PCR Master Mix	0102000014	180.0	
HotStarTaq DNA Polymerase (5 U/µL)	HEA16-12A	4.0	

BIDS XT search function

Allows performing complex searches in the database select the desired number of antigens.



BLOODchip ID

Reagents and Software

REFERENCE	PRODUCT NAME	PRODUCT DESCRIPTION	SIZE
221239	ID CORE XT*	Genetic identification panel for 37 RBC antigens by DNA analysis	48 tests
221238	ID HPA XT*	Genetic identification panel for 12 HPA systems by DNA analysis	48 tests
730001	ID RHD XT*	Genetic identification panel for 6 RHD variants and HPA-1	24 tests
730285	ID CORE CONTROL*	Positive control for ID CORE XT	25 tests
221240	BIDS XT*	BLOODchip ID software XT	1 unit

Equipment

REFERENCE	PRODUCT NAME	PRODUCT DESCRIPTION	SIZE
220973	Luminex 200™ system with xPONENT® software	Luminex 200 system with xPONENT software and PC/flat panel monitor	1 unit

* ID CORE XT, ID HPA XT, ID RHD XT, BIDS XT, and ID CORE CONTROL comply with the Directive 98/79/EC of the European Parliament and of the Council on in vitro diagnostic medical devices. CE mark certification.

ID CORE XT, ID CORE CONTROL and BIDS XT are sold in US as IVD (FDA).

ID HPA XT and ID RHD XT are sold in the US for research use only. Not for use in diagnostic procedures.

Product registration and availability vary by country. Ask your local Grifols representative for more information.

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