Centro de Hemoterapia y Hemodonación de Castilla y León

Junta de Castilla y León

SEI Sociedad Española de Inmunología

External Proficiency Testing for Immunology Labs

GECLID 2027 v1.0

Prospectus: Histocompatibility and Immunogenetics subprogram

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Marked schemes are not under ISO 17043 accreditation

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SUBCONTRACTING

The subcontracting is carried out in accordance with the center's procurement procedures, currently being awarded:

- **Courier:** NACEX, Cl. Cobalto, 13 47012Valladolid, Spain
- **Manteinance of GECLID web:** Fundación General de la Universidad de Valladolid Edificio Rector Tejerina. Universidad de Valladolid Pl. Colegio de Sta. Cruz, 5 47002 Valladolid, Spain
- **Hosting GECLID web:** ARSYS Calle Madre de dios, 21 Logroño 26004 La Rioja, Spain
- **Manteinance of reports' repository:** Splink C / Valle de Arán 9 47010 Valladolid , Spain
- **Homogeneity and stability assays:** Laboratorio del Centro de Hemoterapia y Hemodonación de Castilla y León Paseo de Filipinos s/n 47007 Valladolid, Spain

CONFIDENCIALTY:

Your individual results will be anonymously published together with those of the rest of the laboratories. Both the authorship of each set of results and the evaluation of performance will be accessible only with your username and password in the repository of individual reports.

Centro de Hemoterapia y Hemodonación de Castilla y León will ensure the confidentiality of any information obtained or generated during the organization of the interlaboratory comparison. This information will not be published or disclosed to third parties without prior consent of the participants. If there were a legal

requirement to disclose confidential information, the interested participant will be notified of the information provided, unless prohibited by law.

GLOSSARY

HLA: human leucocyte antigen, major histocompatibility antigen.

EFI: European Federation for Immunogenetics

Consensus: in all serological schemes is required that at least 75% of the participants agree on the results. When no consensus is set, samples will not be evaluated (1).

cells: in this prospectus the term cell is used to refer to peripheral blood samples (diluted buffy coats)

WBC: White blood cells

PBMCs: peripheral blood mononuclear cells

Standard deviation (σ): robust standard deviation of results calculated using the algorithm A of Appendix C STANDARD ISO 13528: 2015.

Standard uncertainty (Ux): measure of the overall dispersion of the parameter data

$$u_x = \frac{1.25 * s^*}{\sqrt{n}}$$

Acceptance range: z-score range between -2 and 2, within this range a result is considered as correct.

Robust mean (assigned value, X): consensus value among participants, is the robust average of the results obtained by all participants, calculated using the algorithm A Annex C - ISO 13528 STANDARD.

Assigned value: value attributed to a parameter of the interlaboratory comparison (2) it can refer both to a result that is decided to be correct by consensus of the participants, or to the ones endorsed by the Steering Committee. Regarding molecular typing schemes, it will be the one with the highest resolution endorsed by any of the members of the Steering Committee, integrated by EFI accredited laboratories

Accepted value: value equivalent to that assigned to a parameter of the sample subject to intercomparison. In the case of typing schemes, they will be those of lower resolution endorsed by one of the members of the Steering Committee or those that are correct without having been informed by the Steering Committee.

Correct result: whole result containing no disagreement with the assigned or accepted value(s).

SCHEMES

For each of the exercises within all schemes, detailed instructions and appropriate information on each sample, test specifications if relevant, units in which the results should be expressed and shipping date will be provided.

Any issues or comments that may arise as running the interlaboratory comparison exercise will be communicated to participants and taken into consideration when evaluating the results.

Table 1 Schemes, and schedules for sending samples and receipt of results for evaluation are summarized. Each shipment is assigned a code number (s) identification (the) schemes which account. In cases where more than one shipping scheme are named as rn (r1, r2…). In Scheme 12 a single shipment of samples is made. The first shipment of Scheme 3A and 3B consists of sera (indicated by s) and the 2 following ones, are the cell ones.

There is, in all schemes, the possibility for laboratories, to register and participate in the exercise Interlaboratory comparison without being evaluated. This feature must be reported to the Head of the Program.

Table 1: Schemes and the program samples Histocompatibility GECLID 2027

SCHEME	PARAMETERS	Samples / round	Rounds / year	Time limit for receipt of results
HLA-2A **HLA-disease 1**	HLA-B27	5 cells	two	6 weeks
HLA-2B **HLA-disease 2**	HLA-B * 57: 01	5 cells	two	6 weeks
HLA-2C **HLA-Disease 3**	HLA susceptibility to celiac disease	5 cells	two	6 weeks
HLA-3A **cytotoxicity crossmatch**	Crossmatch against T and B lymphocytes (IgG reactivity against T and B)	14 sera 2 cells	3 (1 sera, two cells)	2 weeks
HLA-3B **crossmatch cytometry**	Crossmatch against T and B lymphocytes (IgG reactivity against T and B)	14 sera 2 cells	3 (1 sera, two cells)	2 weeks
HLA-4A **Ac detection. anti HLA class I and II**	Ac detection. anti-HLA class I and II	7 sera	two	6 weeks
HLA-4B **Ac detection and analysis. Anti HLA class I and II**	Antibody detection and identification of specific anti HLA class I and II antibodies	7 sera	two	6 weeks
HLA-5AB **Molecular typing HLA-I and II (low resolution)**	HLA Low resolution typing molecular 5A: HLA-A, -B, -C 5B: HLA-DRB1, -DRB3 / DRB4 / DRB5 -DQA1, -DQB1	5 cells	two	6 weeks
HLA-6AB **Molecular typing HLA-I and II (high resolution)**	High resolution typing molecular HLA 6A: HLA-A, -B, -C 6B: HLA-DRB1, -DRB3 / DRB4 / DRB5, -DPB1, -DQA1, -DQB1, (-DPA1)	5 cells	two	8 weeks
HLA-8[#] **chimerism**	Determination of the DNA % in a mixture of two components (individuals)	2 cells 5 mixtures	two	2 weeks
HLA-9 KIR typing	Molecular typing KIR: 2DL1, 2DL2, 2DL3, 2DL4, 2DL5, 2DS1, 2DS2, 2DS3, 2DS4, 2DS5, 2DP1, 3DL1, 3DL2, 3DL3, 3DS1, 3DP1	5 cells	two	6 weeks
HLA-10 antibodies induced by heparin[#]	Anti H-PF4	5 sera	two	12 weeks
HLA-11A HPA typing	HPA-1, 2, 3, 5, 15	5 bloods	two	3 weeks
HLA-11B HNA Typing[#]	HNA-1a, 1b and 1c	5 bloods	two	3 weeks
HLA12A anti-HPA antibodies	anti HPA	5 sera	two	12 weeks
HLA12B anti-HNA antibodies #	anti HNA	5 sera	two	12 weeks
HLA-14A Anti GSTT1[#]	GSTT1 antibodies	2 sera	two	6 weeks
HLA-14B GSTT1Typing[#]	GSTT1 allele	2 bloods	two	6 weeks
HLA-15 cfDNA[#]	Determination of the cf DNA % in a mixture of two components (individuals)	1 mixtures	2	3 months

[#]Marked schemes are not under ISO 17043 accreditation

Table 2: Schedule Subprogram of Histocompatibility and Immunogenetics GECLID 2027

Fecha envio / *Shipping date*		**Ronda/ *Round***	
26/01/2027	*HLA-11A HPA typing*	r	1
26/01/2027	*#HLA-15 cf DNA*	r	1
26/01/2027	*HLA-2A B27*	r	1
02/02/2027	*HLA-12 Anti HPA antibodies*	r	u
02/02/2027	*HLA-3AB Crossmatch sera*	s	
02/02/2027	*HLA-4 Detection and specificity of anti HLA antibodies (class I and II)*	r	1
16/02/2027	*HLA-5AB Low resolution HLA DNA typing*	r	1
16/02/2027	*#HLA-8 Chimerism*	r	1
16/02/2027	*HLA-9 KIR Typing*	r	1
08/03/2027	*HLA-3A Cytotoxicity Crossmatch cells*	r	1
08/03/2027	*HLA-3B Cytometry Crossmatch cells*	r	1
24/03/2027	*HLA-6AB High resolution HLA DNA typing*	r	1
18/05/2027	*HLA-2B B57:01*	r	1
18/05/2027	*HLA-2C DQ2/DQ8*	r	1
13/09/2027	*HLA-4 Detection and specificity of anti HLA antibodies (class I and II)*	r	2
21/09/2027	*HLA-5AB Low resolution HLA DNA typing*	r	2
21/09/2027	*#HLA-8 Chimerism*	r	2
28/09/2027	*HLA-9 KIR Typing*	r	2
18/10/2027	*HLA-6AB High resolution HLA DNA typing*	r	2
09/11/2027	*HLA-2B B57:01*	r	2
09/11/2027	*HLA-2C DQ2/DQ8*	r	2
09/11/2027	*HLA-3A Cytotoxicity Crossmatch cells*	r	2
10/11/2027	*HLA-3B Cytometry Crossmatch cells*	r	3
23/11/2027	*HLA-11A HPA typing*	r	2
24/11/2027	*#HLA-15 cf DNA*	r	2
29/11/2027	*HLA-2A B27*	r	2
26/01/2027	*HLA-11A HPA typing*	r	1

Some dates are approximate, depending on the availability of patients

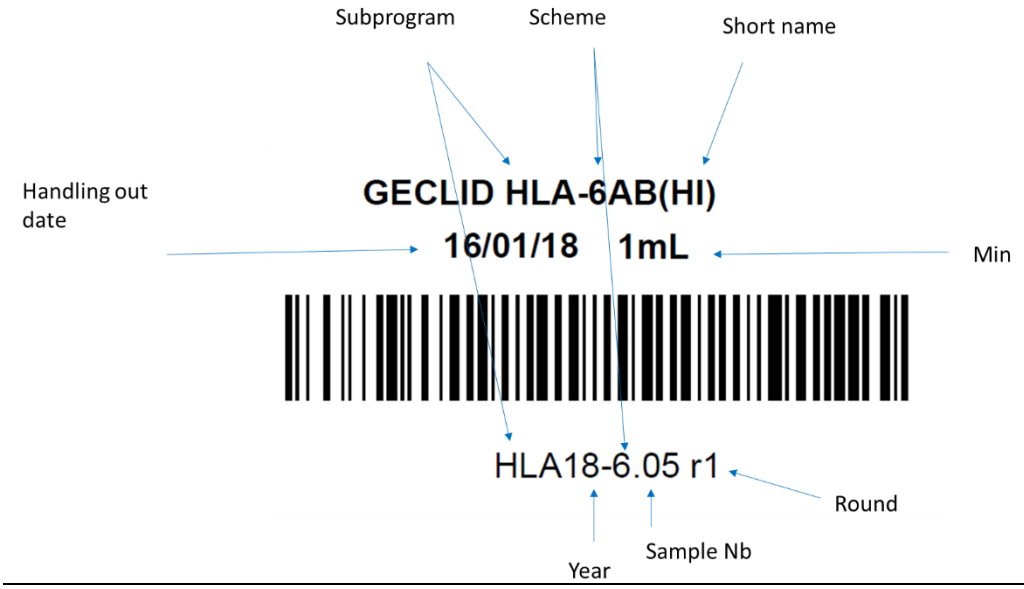
Some schemes are conditioned waiting for confirmation n> 5

#Marked schemes are not under ISO 17043 accreditation

#The possibility exists of requesting samples typed in previous rounds with their corresponding reports to be used as reference materials in the laboratory (not accreditated)

#The possibility exists of requesting extraordinary rounds of typing with individual performance evaluation on samples typed in previous rounds, relabeled and randomized, which will follow the same rules as current rounds of the corresponding scheme(not accreditated)

Sample identification



HLA-2A: HLA-B27

Purpose:

Evaluating the performance of participants in determining carrier status or not regarding HLA- B27 (B * 27).

Sample's distribution:

They will be evaluated at least 10 samples per year with an approximate volume of 2 mL and a cellularity above 6 x 10^6 leukocytes/mL. For this, two shipments will be made with 5 samples each. If it was necessary to discard any of the samples the first shipment, new ones will be added to the second. If necessary, it would be made a third round, ensuring that there are at least 10 evaluable samples on.

Reporting results:

Within this scheme the results recorded as HLA-B27 (B * 27) positive / negative regardless the method by which they were obtained. Optionally and not evaluable, the HLA-B * 27 allele found if positive is recorded. The method is also recorded.

Obtained results can be sent exclusively by means of the web result's form.

Data shall be recorded within 6 weeks of receipt of the samples.

Determination of the assigned value:

The phenotype of the sample will be determined by consensus of at least 75% of the participating laboratories. GECLID ensures that all samples distributed to the participants are typed by molecular methods by the Steering Committee for Histocompatibility and Immunogenetics, integrated by 5 HLA labs, all of them accredited by EFI as shown in section 19.2 of the standard EFI. If necessary, GECLID can adjust the value assigned to the typing, based on the results obtained by molecular biology with the agreement of the Steering Committee.

Scores:

- Each determination of HLA- B27 (B * 27) coinciding with the consensus-assigned value: Ok (0 points)
- Each determination of HLA- B27 (B * 27) does not coincide with the consensus-assigned value: not correct (1 point)
- Each determination of HLA- B27 (B * 27) not tested: not receive rating

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory report at the end of the program (annual) it will be necessary to properly inform all states evaluated.

All participating laboratories will be able to download a certificate of competence for determining HLA-B27 carrier status, no later than 6 weeks from the end of the EPT year.

HLA-2B: HLA-B*57: 01

Purpose:

Evaluating the performance of participants in determining carrier status or not for HLA-B * 57 allele: 01.

Sample's distribution:

They will be evaluated at least 10 samples per year. For this, two shipments will be made with five samples each with a volume of approximately 2 mL and a cellularity above 6 x 10^6 leukocytes/mL. If it was necessary to discard any of the samples of the first shipment, new ones will be added to the second. If necessary, a 3rd round would be carried out, ensuring that there are at least 10 evaluable samples on.

Reporting results:

Within this scheme the results will be recorded as HLA-B * 57: 01 positive / negative. Other B*57 alleles would be optional and not evaluable. The method is also recorded. Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 6 weeks of receipt of the samples.

Determination of the assigned value:

The phenotype of the sample will be determined by consensus of at least 75% of the participating laboratories. GECLID ensures that all samples distributed to the participants are typed by molecular methods by the Steering Committee for Histocompatibility and Immunogenetics, integrated by 5 HLA labs, all of them accredited by EFI as shown in section 19.2 of the standard EFI. If necessary, GECLID can adjust the value assigned to the typing, based on the results obtained by molecular biology with the agreement of the Steering Committee.

Scores:

- Each determination of HLA-B * 57: 01 coincident with the consensus-assigned value: correct (0 points)
- Each determination of HLA-B * 57: 01 not coincident with the consensus-assigned value: incorrect (1 point)
- Each determination of HLA-B * 57: 01 not tested: not receiving rating

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory report at the end of the program (annual) will be necessary to properly inform all states evaluated.

All participating laboratories will be able to download a certificate of competence for determining HLA-B57, no later than 6 weeks from the end of the EPT year.

HLA-2C: HLA susceptibility to celiac disease

Purpose:

Evaluating the performance of participants in determining carrier status or not of combinations of HLA alleles that confer susceptibility to celiac disease: DQA1 * 05 / DQB1 * 02 and others

Sample's distribution:

They will be evaluated at least 10 samples per year. Two shipments will be made with five samples each, with an approximate volume of 2mL and a cellularity above 6 x 10^6 leukocytes/mL. If it was necessary to discard any of the samples the first shipment, new ones will be added to the second. If necessary, a 3rd round would be carried out, ensuring that there are at least 10 evaluable samples on.

Reporting results:

Within this scheme, the results of the HLA allele combinations associated with celiac disease will be recorded as (1) high risk/medium-low risk/no risk (according to their usual practice, some recommendation papers are available at the web)and (2) haplotypes (2.5, 2.2, 8, other). The report will be made exclusively through the Results Form. The report will be sent to GECLID within a period of 6 weeks from receipt of the samples.

Determination of the assigned value:

Both haplotypes and their associated risk will be determined by consensus of at least 75% of the participating laboratories. GECLID ensures that all samples distributed to the participants are typed by molecular methods by the Steering Committee for Histocompatibility and Immunogenetics, integrated by 5 HLA labs, all of them accredited by EFI as shown in section 19.2 of the standard EFI.. If necessary, GECLID can adjust the value assigned to the typing, based on the results obtained by molecular biology with the agreement of the Steering Committee.

Scores:

- Each haplotype or risk related to Celiac disease susceptibility coincident with the consensus-assigned value: Ok (0 points)
- Each haplotype or risk related to susceptibility to celiac disease Mismatch with consensus: not correct (1 point)
- Each haplotype or risk related to susceptibility to celiac disease tested: not receive rating

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory report at the end of the annual program will be necessary to properly inform all states evaluated.

All participating laboratories will be able to download a certificate of competence for determining HLA associated with celiac disease, no later than 6 weeks from the end of the EPT year.

HLA-3A: cytotoxicity crossmatch

Purpose:

To determine the performance of participants in analyzing crossmatches as performed by microlymphocytotoxicity.

Sample's distribution:

A total of 4 samples of cells are to be distributed (with a volume of approximately 4 mL) in two annual shipments of two blood samples (above 6 x 10^6 leukocytes/mL and more than 2 x 10^6 lymphocytes/mL and a viability over 90%) each and 14 sera (with a volume of approximately 0.25 mL) in a single shipment (and common to HLA3B scheme for flow cytometry crossmatch), adding up 56 crossmatches. Each **neat** serum should be tested against all 4 blood samples. Participants must analyze T, B lymphocytes or total mononuclear peripheral blood cells against untreated sera.

Reporting results:

Within this scheme the results will be reported as positive or negative. The results of total mononuclear fraction (cells, whole), that refers to crossmatches performed with this fraction, without T or B lymphocytes' separation, T and B cells are considered separately. Results of manipulated sera can be reported within Notes' field and will not be evaluated.

It is optional, but evaluable, to separately record results for sera treated with DTT against T lymphocytes and B lymphocytes. This option does not exempt laboratories from testing their untreated sera in any case (neither when testing, PBMCs, T or B lymphocytes).

Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 2 weeks of receipt of each shipment of cells.

Determination of the assigned value:

The result of each crossmatch will be determined by consensus at least 75% of the participating laboratories. Those combinations where no consensus is reached will not be evaluable.

Scores:

- Each crossmatch coincident with the consensus-assigned value: Ok (0 points)
- Each crossmatch not coincident with the consensus-assigned value: not correct (1 point)
- Each not tested crossmatch: not receive rating

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory report at the end of the annual program at least 85% of all serum-cell combinations must be informed correctly and must have reported at least 10 sera and 2 cells, ie, a minimum of 20 crosses.

All participating laboratories will be able to download a certificate of competence for crossmatch performing, no later than 6 weeks from the end of the EPT year.

HLA-3B: crossmatch-cytometry

Purpose:

To determine the performance of participants in in analyzing crossmatches as performed by flow cytometry.

Sample's distribution:

A total of four samples of cells in two annual shipments of two blood samples (above 6 x 10^6 leukocytes/mL and more than 2 x 10^6 lymphocytes/mL and a viability over 90%) are distributed (with an approximate volume of 5 mL) each and 14 sera in a single shipment (common to this scheme and the HLA-3A Cytotoxicity, with an approximate volume 0.25mL), making up a total of 56 crossmatches. Each **neat** serum should be tested against all tested populations. Participants will test the peripheral blood samples accordingly to their standard practice, distinguishing antibodies against T and B subpopulations.

Reporting results:

Within this scheme the results will be reported as positive or negative. T and B cells are considered separately. Results of reduced or manipulated sera can be reported within Notes' field and will not be evaluated.

Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 14 days from receipt of each shipment of cells. Results of reduced or manipulated sera can be reported within Notes' field and will not be evaluated

Determination of the assigned value:

The result of the crossmatches will be determined by consensus at least 75% of the participating laboratories. Those combinations where no consensus is reached will not be evaluable.

Scores:

- Each crossmatch coincident with the consensus-assigned value: Ok (0 points)
- Each crossmatch not coincident with the consensus-assigned value: not correct (1 point)
- Each not tested crossmatch: not receive rating

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory report at the end of the annual program at least 85% of all serum-cell combinations must be informed correctly and must have reported at least 10 sera and 2 cells, ie, a minimum of 20 crosses.

All participating laboratories will be able to download a certificate of competence for crossmatch performing, no later than 6 weeks from the end of the EPT year.

HLA-4AB: Detection and identification of specific anti HLA class I and II antibodies

Purpose:

The various techniques used in the investigation of the presence and in the determination of specific antibodies against HLA molecules have different degrees of sensitivity and specificity and they are therefore not comparable. These techniques can be complementary and indeed many laboratories use more than one in routine screening of antibodies. The purpose of this interlaboratory comparison is not to compare techniques, but to evaluate the performance of participants in determining the presence antibodies anti HLA class I and II and the specificities of these with one or more detection techniques.

Sample's distribution:

A total of 14 samples are distributed annually in a single shipment, with an approximate volume of 0.4mL. Within this scheme the specificities of both anti HLA class I and class II antibodies is recorded. However, it is possible to send only results for antibodies against class I or class II, provided such particularity is notified to GECLID before the first delivery of samples.

GECLID ensures that all serum samples to be distributed to participants for detecting anti-HLA antibodies, are tested in advance by CDC by the multicenter reference, the Steering Committee for Histocompatibility and Immunogenetics, or by an EFI accredited lab as shown in section 19.2 of EFI (3) standards

Reporting results:

Obtained results can be sent exclusively by the web results' form and the presence / absence of different antibody specificities against the HLA class I molecules and II included in that form in the section corresponding to the technique or techniques used by the laboratory. Interpretations (Bw, DP, and DQ) are not mandatory although the Steering Committee recommends to fill them in and are evaluable. Data shall be recorded within 6 weeks of receipt of the samples.

Determination of the assigned value:

The presence/absence of antibodies in each sample will be determined by consensus of at least 75% of the participating laboratories for each method[w]. When participants fail to report a specificity on the list, 95% of the laboratories will be required to not reporting the specificity as positive to consider it as negative consensus, as stated in the EFI standards. The specificities that are negative by omission by between 75 and 95% of the participants will be included in the report as non-assessable negatives and will not be penalized. Those parameters where consensus is not reached will not be evaluable. In the parameters in which n<5, the assigned value has merely informative effects (LN, low number), since it is considered that the agreed result is not robust enough to be evaluated. In the particular case of interpretations, it is considered that the laboratories that carry out any of the interpretations of the loci participate for all of them.

Scores:

- Each determination coincident with the consensus-assigned value: Ok (0 points)
- Each determination not consistent with the consensus: not correct (1 point)
- Each determination not tested: not receive rating

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory annual report, it will be necessary to have a minimum of 12 tested sera and to correctly inform at least 75% of the specifics that have reached consensus.

All participating laboratories will be able to download a certificate of their competence for the analysis of specific anti HLA antibodies class I and II, no later than 6 weeks from the end of the EPT year.

[w] CDC determinations are usually under 10 participants and should be therefore, considered a workshop.

HLA-5AB: Typing low-resolution DNA HLA class I / class II

Purpose:

Determining the performance of participants in typing HLA class I (5A) / II (5B) using low resolution molecular methods. This scheme will not regard results for DPA1 and DPB1 loci.

Sample's distribution:

10 samples will be evaluated annually. To do this, 10 samples will be distributed in two batches with 5 samples each, with an approximate volume of 1mL and a cellularity above 6 x 10^6 leukocytes/mL. If it was necessary to discard any of the samples within the first shipment, new ones will be added to the second. If necessary, a 3rd round would be carried out, ensuring that there are at least 10 evaluable samples on.

Reporting results:

Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 6 weeks of receipt of the samples.

The DNA-based typing result will be reported at the level of the digits comprising the first field in the DNA-based nomenclature although –just regarding DRB3, DRB4 and DRB5- reporting as +/- will be accepted.

Determination of the assigned and accepted value(s):

The phenotype of the sample will be determined by consensus of at least 75% of the participating laboratories. GECLID ensures that all samples distributed to the participants are typed by molecular methods by the Steering Committee for Histocompatibility and Immunogenetics, integrated by 5 HLA labs, all of them accredited by EFI as shown in section 19.2 of the standard EFI. If necessary, GECLID can adjust the value assigned or the accepted one(s) to the typing, based on the results by the Steering Committee.

Scores:

5A (class I): For a result to be considered correct, the complete assignment of class I specificities of all loci by a participating laboratory has to be correct.

5B (class II): For a result to be considered correct, the complete assignment of specific class II loci by a participating laboratory has to be correct

- Each matching determination with the assigned or accepted value: right (0 points)
- Each determination is not coincident with the assigned or accepted value: wrong (1 point)
- Each determination not tested: not receive rating

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory report at the end of the annual program will be necessary to properly inform the phenotypes least 9/10 or 90% of the reported samples.

All participating laboratories will be able to download a certificate of competence for the low resolution typing HLA class I / II, no later than 6 weeks after the end of the EPT year.

HLA-6AB: High resolution Typing DNA HLA class I / class II

Purpose:

Determining the performance of participants in typing HLA class I (6A) / II (6B) using molecular high resolution methods.

Sample's distribution:

10 samples will be evaluated annually. To do this, 10 samples will be distributed in two batches with 5 samples each, with an approximate volume of 1mL and a cellularity above 6 x 10^6 leukocytes/mL. If it was necessary to discard any of the samples the first shipment, new ones will be added to the second. If necessary, a 3rd round would be carried out, ensuring that there are at least 10 evaluable samples on.

Reporting results:

Within this scheme results high-resolution class I (Scheme 6A) and / or class II (Scheme 6B) will be recorded. Data will be collected on the sequencing platform, the version of the software, reagents and accessories used.

In Scheme 6A results for class I high resolution typing (minimum two fields) should be based at least on the polymorphism of exons 2 and 3 and excluding any all null alleles, regardless of the location of polymorphisms defining them (3). In Scheme 6B results of high resolution class II typing (minimum two fields) should be based at least in exon 2 polymorphism (3). The P / G nomenclature can be used whenever deemed appropriate by a laboratory to designate indeterminations. However, it should be noted that, if the suffix G is indicated, it must be ensured that the group does not include null alleles or perform the appropriate entry in the observation field of the sample.

Any typing containing null alleles is not accepted as correct unless the list of every null alleles discarded is explicitly recorded. Whenever the information provided in the Notes field is inconsistent with the reported result, the result will be penalized.

Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 8 weeks from receipt of samples.

Determination of the assigned and accepted value (s):

The phenotype of the sample will be determined by consensus of at least 75% of the participating laboratories. The assigned typing is that of maximum resolution typing reported by one of the laboratories of the Steering Committee, provided it is ratified by them as a joint decision. The HLA steering committee will discuss and ratify any assigned or accepted values for each locus in the HLA-6 scheme prior to their publication. GECLID ensures that all samples are distributed to participants will be typed by the laboratory of multi-reference lab, the Steering Committee for Histocompatibility and Immunogenetics, all of them accredited by EFI, in order to decide the outcome of Reference or assigned value. Other typing values equivalent to the assigned one may be included as accepted values, with the approval of the Committee.

In case of discrepant results between two committee members at a resolution level higher than that required for this exercise, the lower resolution typing be assigned, and the two higher-level types will be accepted for reporting purposes. Investigations will continue to clarify the source of the discrepancy. These results will be communicated to the participants as soon as possible.

Scores:

6A: (class I): For a result to be considered correct, the complete assignment of class I alleles of all loci by a participating laboratory has to be correct. 6B: (class II): For a result to be considered correct, the complete assignment of class II alleles of loci by a participating laboratory has to be correct.

- Each name including null alleles not included in the reference typing or assigned value: wrong (1 point)
- Each determination ignoring null alleles included in the results for reference or assigned value: wrong (1 point)
- Each denomination skipping null alleles included in the results for reference or assigned value: not correct (1 point)
- Each matching determination with the assigned or accepted value: right (0 points)
- Each determination that is not coincident with the assigned or accepted value: wrong (1 point)

- Each determination including null alleles not included in the reference typing or assigned value: wrong (1 point)
- Each determination not tested: not receive rating

Only alleles appearing in the last HLA Nomenclature Report (2) and recognized as a year before sending results in databases (5) can be evaluated. If it appeared that some samples did not meet this requirement, it will be properly discussed and explained in the global reports of samples.

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory report at the end of the (annual) program, it will be necessary to properly inform the phenotypes least 9/10 or 90% of the samples of the exercise.

All participating laboratories will be able to download a certificate of competence for high resolution typing HLA class I / II, no later than 6 weeks from the end of the EPT year.

HLA-8: Chimerism#

Purpose:

Determining the performance of participants in the detection of hematopoietic chimerism by determining the ratio of DNA / cells in a mixture of two components (individuals).

Sample's distribution:

10 mixtures are evaluated annually. For this, 10 mixtures were distributed in two batches with 5 more mixes and their 2 individual components (buffy coats anticoagulated with CPD and diluted in RPMI) (simulating studies of 5 transplants). Samples of relatives will be preferred, with a volume of approximately 1 mL and a cellularity above 6 x 10^6 leukocytes/mL. If it was necessary to discard any of the samples in the first shipment, new mixtures will be added to the second. If necessary, a 3rd round would be carried out, ensuring that there are at least 10 evaluable samples on.

Reporting results:

Participants should characterize the individual components of each round with the markers used in their routine assays, which can help distinguish them. These markers should be used to determine the percentages of the minor components in the 5 mixtures of each round.

Presence / absence of the individual components and the percentage of the minor component will be recorded.

Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 2 weeks from receipt of samples.

Determination of the assigned value:

GECLID ensures that all mixtures are distributed to participants will have a traceable formulation from values leukocyte count provided by the center providing the samples and the volume of each specimen used in the sample (formulation values).

The presence of components in the mixture will be determined by consensus at least 75% of the participating laboratories. If this consensus is not reached, it will be assigned the formulation value or quantitative PCR data.

Quantification will be represented by the robust mean of results from participants and its corresponding uncertainty (ISO17043). If the number of participants were n <10, formulation values may be used instead

Scores:

Discrepancies to be considered:

- Reporting no possibility to discern between hypothetical couples receptor/donor 2 points
- Reporting a non-existing component in the mixture (reporting a pure sample as a mixture) 1 point
- Fail to report a component present in the mixture (reporting a mixture as pure sample), if the mixture is above the sensitivity limit of 1 point

For a percentage deemed correct, the z-score value must be within the acceptance range.

Scores:

- Є z (-2, 2) correct result (0 points)
- Є z (-3, -2] U [2, 3) warning: questionable result (1 point)
- Є z (-, -3] U [3,) action signal: incorrect result (2 points)

The accumulation of two or more points on a same parameter within two consecutive rounds evidences the occurrence of anomalies that should be investigated and corrected by the laboratory (4).

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory report at the end of the (annual) program, it will be necessary to obtain two or less points in a same parameter and sending results to 9 samples. All participating laboratories will be able to download a certificate of performance no later than 6 weeks from the end of the EPT year.

HLA-9: KIR Typing

Purpose:

Determining the performance of participants typing KIR (presence / absence of genes) using molecular methods

Sample's distribution:

10 samples will be evaluated annually. To do this, 10 samples will be distributed in two batches with 5 samples each, with an approximate volume of 1mL and a cellularity above 6 x 10^6 leukocytes/mL. If it was necessary to discard any of the samples the first shipment, new ones will be added to the second. If necessary, a 3rd round would be carried out, ensuring that there are at least 10 evaluable samples on.

Reporting results:

Within this scheme results are recorded as presence / absence of KIR 2DL1, 2DL2, 2DL3, 2DL4, 2DL5, 2DS1, 2DS2, 2DS3, 2DS4, 2DS5, 2DP1, 3DL1, 3DL2, 3DL3, 3DS1, 3DP1 genes. Data will be collected about the technology, platform, the version of the software, reagents and accessories used.

Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 6 weeks of receipt of the samples.

Determination of the assigned value:

The phenotype of the sample will be determined by consensus of at least 75% of the participating laboratories. GECLID ensures that all samples distributed to the participants are typed by molecular methods by the Steering Committee for Histocompatibility and Immunogenetics, integrated by 5 HLA labs, all of them accredited by EFI as shown in section 19.2 of the standard EFI. If necessary, GECLID can adjust the value assigned to the typing, based on the results obtained by molecular biology with the agreement of the Steering Committee.

Scores:

- Each determination KIR coincident with the consensus-assigned value: Ok (0 points)
- Each KIR determination not coincident with the consensus-assigned value: not correct (1 point)
- Each not tested determination of KIR: not receive rating

To obtain a satisfactory report at the end of the annual program must correctly inform 9 of the 10 samples sent.

All participating laboratories will be able to download a certificate of competence for typing KIR, no later than 6 weeks from the end of the EPT year.

HLA-10 antiplatelet antibodies induced by heparin [#]

Purpose:

Evaluating the performance of participants in anti-platelet antibodies determination and related type II heparin-induced immune thrombocytopenia.

Sample's distribution:

A total of 5 samples are distributed annually. Within this scheme the results of anti-HPF4 will be informed.

Reporting results:

Obtained results can be sent exclusively by the form Result indicating presence / absence of anti-HPF4 antibodies. Data shall be recorded within 12 weeks from receipt of samples.

Determination of the assigned value:

The presence/absence of antibodies in each sample will be determined by consensus of at least 75% of the participating laboratories for each method. When participants fail to report a specificity on the list, 95% of the laboratories will be required to not reporting the specificity as positive to consider it as negative consensus, as stated in the EFI standards. The specificities that are negative by omission by between 75 and 95% of the participants will be included in the report as non-assessable negatives and will not be penalized. Those parameters where consensus is not reached will not be evaluable. In the parameters in which n<5, the assigned value has merely informative effects (LN, low number), since it is considered that the agreed result is not robust enough to be evaluated.

Scores:

- Each determination coincident with the consensus-assigned value: Ok (0 points)
- Each determination not consistent with the consensus: not correct (1 point)
- Each determination not tested: not receive rating

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory report at the end of the annual program is required to report correct results sent the two samples.

All participating laboratories will be able to download a certificate of competence for the detection of H-PF4 antibodies, no later than 6 weeks from the end of the EPT year.

[w]The number of participants is usually less than 10, so this exercise is considered a workshop. In the parameters in which n<5, the assigned value has merely informative effects, considering that the consensus result is not robust enough to be evaluated.

HLA-11A HPA Typing

Purpose:

Determining the performance of participants in typing platelet antigens using molecular methods

Sample's distribution:

10 samples will be evaluated annually and will be distributed in two batches with 5 samples each with a volume of at least 1mL and a cellularity above 6 x 10^6 leukocytes/mL. If necessary, a 3rd round would be carried out, ensuring that there are at least 10 evaluable samples on.

Reporting results:

Within this scheme results recorded for HPA-1, 2, 3, 4, 5, 15. Platform, version of the software, reagents and accessories used will be recorded as well.

Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 3 weeks from receipt of samples.

Determination of the assigned value:

The phenotype of the sample will be determined by consensus of at least 75% of the participating laboratories. GECLID ensures that all samples distributed to the participants are typed by molecular methods by the Steering Committee for Histocompatibility and Immunogenetics, integrated by 5 HLA labs, all of them accredited by EFI as shown in section 19.2 of the standard EFI. If necessary, GECLID can adjust the value assigned to the typing, based on the results obtained by molecular biology with the agreement of the Steering Committee.

Scores:

- Each determination coincident with the consensus-assigned value: Ok (0 points)
- Each determination not consistent with the consensus: not correct (1 point)
- Each determination not tested: not receive rating

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory report at the end of the annual program will be necessary to properly report 9 of the 10 samples sent.

All participating laboratories will be able to download a certificate of competence for typing HPA / HNA, no later than 6 weeks from the end of the EPT year.

All participating laboratories will be able to download a certificate of competence for typing HPA / HNA, no later than 6 weeks from the end of the EPT year.

[W] The number of participants is usually less than 10, so this exercise is considered a workshop. In the parameters in which n<5, the assigned value has merely informative effects, considering that the consensus result is not robust enough to be evaluated.

HLA-11B HNA Typing [#]

Purpose:

Determining the performance of participants in the neutrophil antigen typing using molecular methods

Sample's distribution:

10 samples will be evaluated annually. To do this, 10 samples will be distributed with a volume of at least 1mL and a cellularity above 6 x 10^6 leukocytes/mL. If necessary, a 3rd round would be carried out , ensuring that there are at least 10 evaluable samples on.

Reporting results:

Within this scheme results recorded for HNA-1a, 1b and 1c. Data will be collected from the technology platform, the version of the software, reagents and accessories used.

Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 3 weeks from receipt of samples.

Determination of the assigned value:

The phenotype of the sample will be determined by consensus of at least 75% of the participating laboratories. GECLID ensures that all samples distributed to the participants are typed by molecular methods by the Steering Committee for Histocompatibility and Immunogenetics, integrated by 5 HLA labs, all of them accredited by EFI as shown in section 19.2 of the standard EFI. If necessary, GECLID can adjust the value assigned to the typing, based on the results obtained by molecular biology with the agreement of the Steering Committee.

Scores:

- Each determination coincident with the consensus-assigned value: Ok (0 points)

- Each determination not consistent with the consensus: not correct (1 point)
- Each determination not tested: not receive rating

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory report at the end of the annual program will be necessary to properly report 3 of the 4 samples sent.

All participating laboratories will be able to download a certificate of competence for HNA typing, no later than 6 weeks from the end of the EPT year.

wThe number of participants is usually less than 10, so this exercise is considered a workshop. In the parameters in which n<5, the assigned value has merely informative effects, considering that the consensus result is not robust enough to be evaluated.

HLA-12A: Detection and identification of specific anti HPA antibodies

Purpose:

Evaluating the performance of participants in determining the presence antibodies anti HPA and the specificities thereof.

Sample's distribution:

A total of 5 samples distributed annually is a single shipment, with an approximate volume of 0.4mL. Within this scheme the specificities of anti HPA antibodies detected by ELISA and / or techniques Luminex type recorded.

Reporting results:

Obtained results can be sent exclusively by the form Result and therefore the presence / absence of the different specificities of antibodies to HPA antigens included in that form in the section corresponding to the technique or techniques used by the laboratory evaluated. Data shall be recorded within 6 weeks of receipt of the samples.

Determination of the assigned value:

The presence/absence of antibodies in each sample will be determined by consensus of at least 75% of the participating laboratories for each method. When participants fail to report a specificity on the list, 95% of the laboratories will be required to not reporting the specificity as positive to consider it as negative consensus, as stated in the EFI standards. The specificities that are negative by omission by between 75 and 95% of the participants will be included in the report as non-assessable negatives and will not be penalized. Those parameters where consensus is not reached will not be evaluable. In the parameters in which n<5, the assigned value has merely informative effects (LN, low number), since it is considered that the agreed result is not robust enough to be evaluated.

Scores:

- Each determination coincident with the consensus-assigned value: Ok (0 points)
- Each determination not consistent with the consensus: not correct (1 point)
- Each determination not tested: not receive rating

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory annual report will be necessary to have tested 90% of the sera sent and correctly informing the least 75% of the specifics that have reached consensus.

All participating laboratories will be able to download a certificate of competence for antibodies anti HPA analysis, no later than 6 weeks from the end of the EPT year.

wThe number of participants is usually less than 10, so this exercise is considered a workshop. In the parameters in which n<5, the assigned value has merely informative effects, considering that the consensus result is not robust enough to be evaluated.

HLA-12B: Detection and identification of specific anti HNA antibodies[#]

Purpose:

Evaluating the performance of participants in determining the presence antibodies anti HPA and the specificities thereof.

Sample's distribution:

A total of 5 samples distributed annually is a single shipment, with an approximate volume of 0.4mL. Within this scheme the specificities of anti HNA antibodies detected by ELISA and / or techniques Luminex type recorded.

5 total annual samples will be distributed in a single shipment, with an approximate volume of 0.4 mL.

Reporting results:

Obtained results can be sent exclusively by the form Result and therefore the presence / absence of the different specificities of antibodies to HPA antigens included in that form in the section corresponding to the technique or techniques used by the laboratory evaluated. Data shall be recorded within 6 weeks of receipt of the samples.

Determination of the assigned value:

The presence/absence of antibodies in each sample will be determined by consensus of at least 75% of the participating laboratories for each method. When participants fail to report a specificity on the list, 95% of the laboratories will be required to not reporting the specificity as positive to consider it as negative consensus, as stated in the EFI standards. The specificities that are negative by omission by between 75 and 95% of the participants will be included in the report as non-assessable negatives and will not be penalized. Those parameters where consensus is not reached will not be evaluable. In the parameters in which n<5, the assigned value has merely informative effects (LN, low number), since it is considered that the agreed result is not robust enough to be evaluated.

Scores:

- Each determination coincident with the consensus-assigned value: Ok (0 points)
- Each determination not consistent with the consensus: not correct (1 point)
- Each determination not tested: not receive rating

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory annual report will be necessary to have tested 90% of the sera sent and correctly informing the least 75% of the specifics that have reached consensus.

All participating laboratories will be able to download a certificate of competence for antibodies anti HNA analysis, no later than 6 weeks from the end of the EPT year.

[w]The number of participants is usually less than 10, so this exercise is considered a workshop. In the parameters in which n<5, the assigned value has merely informative effects, considering that the consensus result is not robust enough to be evaluated.

HLA-14A Anti GSTT1 antibodies

Purpose:

Evaluating the performance of participants in anti GSTT1 antibodies determination

Sample's distribution:

A total of 4 samples to be distributed annually with at least 250uL serum. Within this scheme the results of anti GSTT1 antibodies will be reported.

Reporting results:

Obtained results can be sent exclusively by the form Result indicating presence / absence of anti GSTT1 antibodies and optionally the obtained absorbance. Data shall be recorded within 6 weeks of receipt of the samples.

Determination of the assigned value:

The presence / absence of antibodies in each sample is determined by consensus at least75% of the participating laboratories. Those samples where no consensus is reached or n <2 for a technique will not be evaluable.

Scores:

- Each determination coincident with the consensus-assigned value: Ok (0 points)
- Each determination not consistent with the consensus: not correct (1 point)
- Each determination not tested: not receive rating

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.
To obtain a satisfactory report at the end of the annual program is required to report correct results for 3 of the 4 samples sent.
All participating laboratories will be able to download a certificate of competence for the detection of anti GSTT1 antibodies, no later than 6 weeks from the end of the EPT year.
wThe number of participants is usually less than 10, so this exercise is considered a workshop. In the parameters in which n<5, the assigned value has merely informative effects, considering that the consensus result is not robust enough to be evaluated.

HLA-14B GSTT1 Typing#

Purpose:

Determining the performance of participants in GSTT1 allele discrimination between silent and expressed allele using molecular methods

Sample's distribution:

4 samples are evaluated annually in two batches with 2 samples each with at least 1 mL whole blood and a cellularity above 6 x 10^6 leukocytes/mL.

Reporting results:

Within this scheme results recorded for the GSTT1 allele. Data will be collected from the technology platform, the version of the software, reagents and accessories used.

Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 6 weeks of receipt of the samples.

Determination of the assigned value:

GECLID ensures that all samples distributed to the participants are typed by molecular methods by the Steering Committee for Histocompatibility and Immunogenetics, integrated by 5 HLA labs, all of them accredited by EFI as shown in section 19.2 of the standard EFI. The phenotype of the sample will be determined by consensus of at least 75% of the participating laboratories. If necessary, GECLID can adjust the value assigned to the typing, based on the results obtained by molecular biology with the agreement of the Steering Committee.

Scores:

- Each determination coincident with the consensus-assigned value: Ok (0 points)
- Each determination not consistent with the consensus: not correct (1 point)

Each determination not tested: not receive rating

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory report at the end of the annual program will be necessary to properly report 3 of the 4 samples sent.

All participating laboratories will be able to download a certificate of competence for typing GSTT1, no later than 6 weeks from the end of the EPT year.

wThe number of participants is usually less than 10, so this exercise is considered a workshop. In the parameters in which n<5, the assigned value has merely informative effects, considering that the consensus result is not robust enough to be evaluated.

HLA-15: cf DNA#

Purpose:

To determine the performance of participants in the detection of cell-free DNA (cfDNA) by determining the proportion of DNA in a mixture of two components (individuals).

Sample's distribution:

Four mixtures will be evaluated annually. For this purpose, two mixtures will be distributed in two shipments with an approximate volume of 5 mL and at least 65 pg/uL of DNA.

Reporting results:

Within this framework, the results for both mixtures will be recorded: total circulating cf DNA and %cf DNA.

The report must be submitted exclusively using the Results Form. The report must be sent to GECLID within 3 months (90 days) weeks after receiving the samples.

Determination of the assigned value:

GECLID guarantees that all mixtures distributed to participants will have a formulation traceable from the leukocyte count values provided by the sample-supplying center and the volumes of each specimen used in the sample (formulation values). Quantification will be represented by the robust mean of the participants' results and its corresponding uncertainty (ISO 17043). If the number of participants is n < 10, the formulation values may be used.

Scores:

For a percentage deemed correct, the z-score value must be within the acceptance range.

Scores:

- Є z (-2, 2) correct result (0 points)
- Є z (-3, -2] U [2, 3) warning: questionable result (1 point)
- Є z (∞, -3] U [3, ∞) action signal: incorrect result (2 points)

The accumulation of two or more points on a same parameter within two consecutive rounds evidences the occurrence of anomalies that should be investigated and corrected by the laboratory (4).

The Steering Committee may request additional evidence from participants if deemed appropriate and / or declare an inconclusive result.

To obtain a satisfactory report at the end of the (annual) program, it will be necessary to obtain two or less points in a same parameter and sending results to 2 samples. All participating laboratories will be able to download a certificate of performance no later than 6 weeks from the end of the EPT year.

ANNEX: STANDARDS GECLID / EFI ASSIGNMENTS FOR recording HLA by DNA (low resolution):

By GECLID, with the knowledge and support of the Steering Committee for Histocompatibility and Immunogenetics have been set some very basic questions for the recording of low resolution HLA typings. The reasons are basically two:

- *Comply with the relevant regulations of the EFI*
- *Make it easier to input results and subsequent analysis of them, minimizing errors.*

Practical issues / TECHNICAL:

*1. NEVER acronym HLA or indicate the name of the HLA locus, or the asterisk * in the results field (already included in the question), so you must directly enter the number of the assigned allele.*

2. There are split responses (allele 1 and alelo2): please always indicate in the field allele 1 that of lower number.

OFFICIAL NOMENCLATURE:

1 In this level (low resolution DNA) only low resolution alleles are ordered. Laboratories who introduce 4 or more digits will not be penalized if the first 2 coincide with the final typing assigned.

2 In particular loci DRB3, DRB4 and DRB5, alleles can be specified as low resolution but is considered also acceptable (for this level of resolution only) to indicate the presence of an allele of these loci using the + symbol.

*3 For apparently homozygous results notation should be p. eg .: B * 07, - or B * 07, B * none but NEVER 07,07.*

4 Serological designations are never accepted (e.g. DR-52) as valid. For the same reason, no data will be recorded for Bw4 / Bw6.

STANDARDS GECLID / EFI for recording DNA ASSIGNMENTS by HLA (high resolution):

By GECLID, with the knowledge and review of the Steering Committee for Histocompatibility and Immunogenetics they are reviewed on a regular basis the system recording of high-resolution HLA typings in order to:

- *Comply the relevant regulations of the EFI*
- *Make it easier the input and analysis of results, minimizing errors.*

PRACTICAL ISSUES:

1. Don't record "HLA", the name of the HLA locus, or the asterisk "" in the results field, you must directly enter the number of the assigned allele.*

2. Always indicate in the field "allele 1" those of lower numbers.

OFFICIAL NOMENCLATURE:

1. At this level EFI standard resolution calling for 2 fields excluding nulls. Laboratories who introduce more digits will take the risk of penalty if their typing does not match the assigned or accepted typing(s).

2. The notation used should be the official of the WHO in its current version, using ALWAYS colon ":" as separators, for example 01:02 and not 0102 (pre-2010 nomenclature).

3. For apparently homozygous results notation should be eg: 29: 02, - or 29:02, "none" but NEVER 29: 02.29: 02 (unless evidence is taken by family segregation which are two different alleles).

4. Ambiguities groups P and G should be used only when appropriate. If a G group contains null alleles, reporting it is considered a mistake unless indicating that nulls have been excluded.

5. Never serological designations are accepted (eg .: DR-52).

COMMON MISTAKES:

- *Use inconsistent P ambiguities (non-existent).*
- *Using the suffix G with 2-digit fields*
- *Suffix G including null alleles that are not specifically excluded*
- *Apparent homozygotes writing twice the name of the allele (should be written only in the allele 1 and allele 2 encode as "none" or "-")*

CRITERIA / ELIGIBILITY

One single registration shall be received by laboratory and subprogram for the purposes of calculating the consensus. For all schemes, laboratories participating in this sub-program should include their own positive and negative controls.

For schemes 1A and 1B only the loci tested by serological methods will be contemplated. Additional techniques may be used to confirm the assignment of specificities.

DNA typing for high resolution, HLA alleles of class I based on exons 2 and 3 at least and class II based on exon 2 ambiguities must be resolved (3).

All participants should note the method used in the site provided for this purpose on the form.

Although there are mandatory parameters in the web forms, each laboratory will decide which are those parameters they need, all reported parameters are evaluable but Notes.

Laboratories not following the instructions regarding the analysis of the samples sent may be excluded from the determination of the assigned /accepted value, without prejudice to possible penalties.

LABORATORY

The laboratory responsible for the handling and distribution of samples and evaluating test results is the QA Immunology Laboratory of the Centro de Hemoterapia y Hemodonación de Castilla y Leon, Valladolid, Spain

SAMPLES specimens or items

Samples

Samples of this subprogram are always of human origin, with minimal handling, so that they are as similar as possible to the usual practice of diagnostic laboratories. The methods employed in the preparation and

distribution of samples have shown (Workshops SEI) to be suitable to ensure uniformity and stability in the conditions listed.

Samples are mostly peripheral blood (buffy coats). They are distributed in aliquots of approximately 1 mL in most cases, this volume will increase to schemes that require separation of lymphocytes. All the manipulation is performed under sterile conditions. Samples will be maintained and sent at room temperature within a period of 36h from extraction. They should be used in up to 24 hours of receipt, after this time, we cannot ensure its viability and stability.

All samples whatever type they are, have been tested for infectious agents before delivery, ensuring that in case of positive serological tests laboratories are informed immediately. If so, GECLID will withdraw the sample from the interlaboratory comparison exercise, replacing it with another. In general, even if all of the panel proposed serologic tests were negative, all samples should be handled, as in clinical practice, as potentially infectious.

Sample Types

BLOOD DONORS SAMPLES: Predictably healthy but are also analyzed to exclude infectious diseases.

PATIENT SAMPLES: By collaborating centers. The samples distributed in the sub-programs and schemes can be obtained from different blood banks and Clinical Services of the Spanish territory in accordance with current legislation on the subject.

Obtention

Most of the samples included in this subprogram are from Biobanks, although laboratories participating in the subprograms and schemes offered, may negotiate with GECLID including local samples (sera, blood) of patients in any of the schemes quality (especially when diagnoses are infrequent or relevant) in accordance with the Manual Partners. For this inclusion shall provide all data to allow traceability of the samples, safety (negative serological tests for infectious agents applicable) and compliance with applicable regulations and associated clinical information.

Sampling will be performed according to the protocol of Partners / Biobank centers after the corresponding informed consent of the donor.

Processing

Samples are processed in appropriate environmental conditions to preserve its integrity (room temperature handling and laminar flow hood when required).

Transport

All samples will be distributed in suitable packaging, in accordance with IATA standard and accompanied by documentation (pdf documents sent by e-mail for the sake of a better sustainability) including at least: the sample number and lot, additives and / or preservatives containing and analytical tests expected to be carried out on each sample by participant laboratories.

All samples included in quality schemes have a documented traceability system: origin, serology, staff has handling and packaging, date of extraction and shipping, etc.

GECLID will keep for at least one year a part of each batch of samples, so that laboratories can acquire on request extra volumes (paying the costs) and can reanalyze them, if necessary.

STATISTICAL METHODS AND SCORING SYSTEMS

Detailed in each of the schemes, we remind the participants that the accumulation of two or more points on the same parameter in two consecutive rounds evidences the occurrence of anomalies that should be investigated and corrected by the laboratory (2). The criteria for Scores will be reviewed annually by GECLID on the basis of the quality standards for providers of interlaboratory comparison (4) and the recommendations of ENAC.

REPORTS

All reports of this subprogram will be issued in English to facilitate their EFI audits. The reports are comprehensive and clear, including both numerical data and graphics to facilitate understanding and interpretation of the results. When they were available, they will also include data tracking. The use of combined scores for various schemes (4) is avoided. For each scheme is issued:

- Global Samples' Report: a descriptive study of all collected data and conclusions. They include, whenever there are at least 10 participants, results stratified by methods of analysis and, at the end of them, the LEM report (laboratories, equipment and methods) collecting the frequencies of participation, methods and reagents used

- Results of individual participation in the Interlaboratory comparison and obtained scores

Each participating laboratory will be identified in these reports exclusively through its unique code. In no case laboratories will be sorted by their performance. These reports will be issued / published by GECLID in the foreseeable period of 2 weeks from the end of each round Interlaboratory comparison for each scheme. Late laboratories will receive an annotation to this respect on the cover of their individual report.

Laboratories may download their reports from each round, and the annual summary evaluation in electronic format (PDF) at https://geclid.centrodehemoterapiacyl.es. This certificate shall be issued by GECLID in a period not exceeding six weeks from the end of the EPT year. Laboratories that request it, can obtain a certificate of participating schemes before the end of the EPT year, data within the certificate will not contain punctuation or evaluation.

Participating laboratories will be responsible for their documentation related to the program and interlaboratory comparisons is kept available for auditors or inspectors of accrediting agencies (ENAC, etc ...) that apply to them.

APPEAL AND COMPLAINTS POLICY

To formalize a claim, complaint or to appeal an evaluation, you must fill in the model document available on the website and email it to direccion.chem@saludcastillayleon.es. Complaints will be managed by the administration at Centro de Hemoterapia. Your appeal or any issue related to reports, results and evaluations will be first reviewed by the quality manager together with the immunologist of GECLID programme, Then by the Steering Committee and finally by the Quality Commission of the Spanish society for immunology (Comisión de Calidad para la Inmunología Diagnóstica (CCID)). You will be informed all along the appeal or complaint progress. Remember that the deadline for appealing ends up 1 month after reports are published.

If the appeal is related to transcription errors of results, you should always provide the original records of the analysis. Appeals are sent to the appropriate Steering committees.

ASSESSMENT of ANNUAL PERFORMANCE

The annual evaluation will be objective, ie, it will be held against targets external quality, defined in this case by the EFI (3, 4). To obtain a satisfactory report at the end of the program (annual) in each scheme, you will need to properly inform at least:

- 90% of the samples for HLA typing schemes (1A, 1B, 5A, 5B, 6A, 6B, 11A)
- all samples for schemes 2A, 2B, 2C, 10, 15
- 85% of the combinations for crossmatch (3A, 3B)
- 75% of the specific anti-HPA antibodies (12A)
- 80% of detections of anti HLA (4A), 80% of identifications (HLA-4B)

All participating laboratories can download a certificate with the assessment of their performance for each of their schemes, no later than 6 weeks from the end of the EPT year. The laboratory can claim about their assessment within 20 working days from receipt of notice thereof.

The criteria for assessment of laboratories will be reviewed annually by GECLID based on the Rules for External Quality Assurance Providers of EFI (1), as well as quality standards for providers of interlaboratory comparison (4).

REFERENCES

1. Standards for PROVIDERS of External Proficiency Testing (EPT) schemes – Version 7.3, 2021
2. Marsh SGE, Osoegawa K, Bodmer WF, Bontrop RE, Carrington MN, Erlich HA, Heidt S, Holdsworth R, Mayr WR, Maiers M, Parham P, Petersdorf EW, Robinson J, Trowsdale J, Fernández-Viña M. Nomenclature for Factors of the HLA System, 2026. HLA. 2026 Mar;107(3):e70595. doi: 10.1111/tan.70595. PMID: 41742599; PMCID: PMC12936402.
3. Standards for Histocompatibility testing v 8.1, 2023 European Federation for Immunogenetics.
4. ISO-IEC 17043:2023 Conformity assessment. General requirements for Proficiency Testing. International Organization for Standardization, 2023
5. ISO 13528:2022 Statistical methods for use in proficiency testing by interlaboratory comparisons
6. http://www.ebi.ac.uk/imgt/hla/ (Release 3.65 (2026-07) Version Report - Build e810882)