External Proficiency Testing for Immunology Labs

GECLID-SIC&SEI 2026 v1.0

Prospectus:
Cellular Immunity Subprogram

CONTACT INFORMATION

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SUBCONTRACTING

Subcontracting is carried out in accordance with the center's procurement procedures, and the current contractors are:

- **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

CONFIDENTIALITY:

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 This information will not be published or disclosed to third parties without prior consent of the participants.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

CAT: The CAT Foundation is a certification organization in the field of transfusion medicine, cell and tissue therapy, made up of the Spanish Society of Hematology and Hemotherapy and the Spanish Society of Blood Transfusion and Cell Therapy, which has a Board of Trustees and a Technical Committee

CD: cluster of differentiation, surface antigen.

CPD: anticoagulant, citrate, phosphate and dextrose solution

Consensus: In all diagnostic schemes, 75% of participants must agree on the results. If the established consensus is not reached for any result, the reference result will be used.

EDTA: anticoagulant, ethylene diaminetetraacetic acid

HepNa: anticoagulant, sodium heparin

Standard deviation (σ): Robust standard deviation of the results, calculated by applying algorithm A of appendix C ISO 13528.

MRD: Minimal residual disease

Standard uncertainty (Ux): measure of the global dispersion of the parameter

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

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

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

Reference result: It will be determined by a consensus of experts, understood as those laboratories that obtained the best scores in the previous rounds.

Correct result: result matching the assigned value or whose z-score is within the acceptance interval.

Assigned value: value attributed to a parameter of the sample subject to interlaboratory comparison (1). In this Prospectus we will refer to both the result that is decided as correct by consensus of the participants, and the reference result.

z-score: value that indicates the positioning of the individual result relative to the overall group result

$$z = \frac{(x - X)}{\hat{\sigma}}$$

SCHEMES

Each exercise in the schemes will be provided with precise and appropriate instructions, including information of each sample, test specifications if relevant, units in which the results must be expressed, and the date of submission.

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

Table 1 lists the schemes of the Subprogram, and Table 2 lists the schedule for sending samples and receiving results for evaluation. Each shipment is assigned a code with the identification number(s) of the scheme(s) to which it corresponds. In cases where there is more than one shipment per scheme, they are designated with the letter r followed by the round number (r1 for the 1st, r2 for the 2nd, etc.).

In all schemes, laboratories have the option to register and participate in the interlaboratory comparison exercise, receiving their scores, but without being evaluated. This detail must be communicated to the GECLID team before the first shipment of samples for the scheme.

Table 1: Schemes of Cellular Immunity Subprogram GECLID 2026

SCHEME	PARAMETERS	SAMPLES /round	ROUNDS /year	Timeframe for results
IC-1 Lymphocytes (count and percentage)	T lymphocyte count and percentage (CD3+); Th (CD3+/CD4+); Tc (CD3+/CD8+); NK (CD3-/CD16+/CD56+); B (CD19)	5 PB	2	2 weeks
IC-2 Stem cells	CD34 cell count and percentage, total viability and CD34 viability	3 UCS/ PB	2	2 weeks
IC-3 Residual Leukocytes	Absolute residual leukocyte count in leukoreduced blood preparations, evaluation of the preparations	2 plasmae 2 red blood cells units 2 platelet units	2	2 weeks
IC-48 Phenotyping and Diagnosis of Leukemias/Lymphomas and MRSD	Positivity/negativity and intensity of expression on a panel of antigens reviewed annually by the Cellular Immunity Steering Committee. Proportion of the leukemic population in the tested sample. WHO diagnosis	2 PB/BM	3	2 weeks
IC-5 Lymphocyte Function	Proliferative response to PHA, ATP production in response to PHA	3 PB	2	2 weeks
IC-6 Innate function	Phagocytosis of monocytes and granulocytes. Burst of monocytes and granulocytes.	3 PB	2	2 weeks
IC-7 Molecular leukemias	IgH and TCR rearrangement; BCR-ABL-p210 (quantitative); BCR-ABL-p190 (qualitative and/or quantitative); PML-RARA (qualitative and/or quantitative); Flt3 (ITD and TDK, qualitative), CALR, MPL, Jak2 exon 12	2 PB	3	4 weeks
IC-9 Monitoring anti-CD20 therapy (rituximab)	Percentage of B lymphocytes (CD19, CD20), memory cells and plasmablasts	3 PB	2	2 weeks
IC-10 PD1* Lymphocytes	PD1-positive lymphocytes in solid tumors %PD1+CD8+ or %PD1CD4+	3 PB	2	2 weeks
IC-11 T* Repertoire	T subfamilies	3 PB	2	2 weeks

IC-12: Advanced T and B Phenotype NEW!*	naïve T and B lymphocytes, effector, regulatory, memory, activated, plasmablasts and transitional	2 PB	2	2 weeks
IC-13: Ploidy and Cell Cycle NEW!*	evaluation of aneuploidy and cellular DNA content by flow cytometry	1 PB (shared with scheme IC-14)	2	2 weeks
IC-14: MLPA-LLA NEW!*	detection of abnormal copy number changes (insertions or deletions) of genomic sequences by ligation-dependent multiple probe amplification	1 PB (shared with scheme IC-13)	2	2 weeks
IC-15: BAL Populations NEW!*	Cell populations in bronchoalveolar lavage (BAL): Total lymphocytes, CD4 T lymphocytes, CD8 T lymphocytes, CD4/CD8 ratio, neutrophils, alveolar macrophages, eosinophils, and Langerhans cells	2 PB	2	2 weeks
IC-17 CAR-T Therapy Monitoring NEW!*	CAR and B lymphocytes in patients treated with Chimeric Antigenic Receptor therapy	1 PB	2	2 weeks

*The new schemes will begin when a minimum of 5 participants is reached

Table 2: GECLID Cellular Immunity Subprogram Calendar2026 (Dates have not yet been assigned to the IC-16 CAR-T Monitoring scheme)

24/02/2026	**r1G1**	**IC-1 Lymphocyte populations**
	r1	**IC-15 Populations in Bronchoalveolar Lavage**
10/03/2026	**r1G2**	**IC-1 Lymphocyte populations**
	r1	**IC-12 Advanced Phenotype T and B**
	r1	**IC-3 Residual leukocytes**
17/03/2026	**r1**	**IC-13 Ploidy and cell cycleC**
	r1	**IC-14 MLPA LLAC**
25/03/2026	**r1**	**IC-2 Stem cells**
	r1	**IC-48 Phenotype, diagnosis and minimal residual disease in oncohematopoietic pathology**
18/05/2026	**r3**	**IC-5 Lymphocyte function**
	r1	**IC-6 Innate Function**
26/05/2026	**r1**	**IC-7 Molecular leukemias**
	r1	**IC-9 Monitoring anti-CD20 therapy (Rituximab)**
24/06/2026	**r2**	**IC-48 Phenotype, diagnosis and minimal residual disease in oncohematopoietic pathology**
30/09/2026	**r2**	**IC-7 Molecular leukemias**
13/10/2026	**r2G1**	**IC-1 Lymphocyte populations**
	r2	**IC-15 Populations in Bronchoalveolar Lavage**
14/10/2026	**r2**	**IC-2 Stem cells**
27/10/2026	**r2**	**IC-13 Ploidy and cell cycleC**
	r2	**IC-14 MLPA LLAC**
10/11/2026	**r2G2**	**IC-1 Lymphocyte populations**
	r2	**IC-12 Advanced Phenotype T and B**
	r2	**IC-3 Residual leukocytes**
11/18/2026	**r3**	**IC-48 Phenotype, diagnosis and minimal residual disease in oncohematopoietic pathology**
23/11/2026	**r2**	**IC-5 Lymphocyte function**
	r2	**IC-6 Innate Function**
01/12/2026	**r3**	**IC-7 Molecular leukemias**
16/12/2026	**r2**	**IC-9 Monitoring anti-CD20 therapy (Rituximab)**

* Some dates are approximate and may depend on patient availability.

[c]Some schemes are conditional pending confirmation that n>5

Sample identification

IC-1: Lymphocytes

Purpose:

Evaluate the performance of participants in the analysis of populations: CD45+, CD3+ lymphocytes, CD19+, NK cells, CD3+ CD4+ subpopulations, CD3+ CD8+

Sample distribution:

Ten samples per year will be evaluated (generally anticoagulated peripheral blood).The anticoagulant or treatment will be indicated with the round information. These samples will be distributed in two shipments of 5 samples each. Participants will be divided into two groups, G1 and G2, which will receive different batches of samples on different dates. Participants may register for both groups to have a greater number of annual controls. The approximate volume of each aliquot is 500 µL. Participants may request additional aliquots by indicating this on their registration form or by emailing the program coordinator.

Results Report:

Results will be recorded of percentage and count of CD3+, CD19+, and NK cells (CD3+ CD4+ and CD3+ CD8+ subpopulations). Reporting the percentage of CD4+ and CD8+ cells is mandatory, it is optional to report the remaining percentages and absolute numbers. Each laboratory will report its results using the form at https://www.geclid.es/ .

All percentages refer to the total lymphocyte count. Referring CD3+CD4+ or CD3+CD8+ percentages to other parameters may result in penalties. Absolute numbers are always reported in cells/µL; using other units may result in penalties.

The Steering Committee recommends NOT assuming that all NK cells are CD3-CD56+CD16+ cells. It should be considered that a fraction of NK cells express CD56 on their membrane but do not express CD16 (the majority of the population known as CD56bright).

The results will be reported to GECLID within 2 weeks from the receipt of the samples.

Determining the assigned value:

The quantification will be represented by the robust mean of the participants' results and its corresponding uncertainty.

Scores and Evaluation:

For a result to be considered correct, its z-value must be within the acceptance interval.

Scores:

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

For the calculation, σ=0.3 will be applied as a limit to the SD initially calculated in all parameters of this scheme as indicated by the SEI-SIC Joint Steering Committee on Cellular Immunity.

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points for any given parameter and to have submitted complete results for 9 of the samples. All participating laboratories will be able to download their certificate of competence for the determination of lymphocyte populations within 6 weeks of the end of the annual period.

IC-2: Stem cells

Purpose:

Evaluate the performance of participants in the analysis of CD34+ stem cell populations.

Sample distribution:

Six CPD-anticoagulated samples will be evaluated annually, distributed in two shipments of three samples each. The approximate volume of the aliquots is 0.6 mL.

Results Report:

Within this framework, only CD34+ cell counts will be evaluated. Reporting percentages is mandatory, while reporting absolute counts, as well as the percentages of lymphocytes, monocytes, and granulocytes, is optional and will be collected for informational purposes only. Each laboratory will report its results using the form at https://www.geclid.es/.

For viability, the percentage of viable CD45 cells in total CD45 cells will be recorded. The percentage of CD34+ cells should refer to the total number of viable CD45+ cells. The number of events should not include spheres.

The results will be reported to GECLID within 2 weeks of receiving the samples.

Determining the assigned value:

The quantification will be represented by the robust mean of the participants' results and its corresponding uncertainty.

Scores and Evaluation:

For a result to be considered correct, its z-value must be within the acceptance interval.

Scores:

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

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points for any one parameter and to have submitted complete results for 5 of the samples. All participating laboratories will be able to download their certificate of competence for the determination of CD34+ stem cells within 6 weeks of the end of the annual exercise.

IC-3: Residual leukocytes

Purpose:

To evaluate the performance of participants in detecting and counting residual leukocytes in different leukoreduced blood preparations. The approximate volume of the aliquots is 250 µL.

Sample distribution:

Twelve samples will be evaluated annually, distributed in two shipments of six samples each (two plasmas, two platelet preparations, and two red blood cell preparations). The approximate volume of the aliquots is 500 µL.

Results Report:

White blood cell count results (cells/µL) will be collected. The report will be sent to GECLID within 2 weeks of receiving each shipment.

Determining the assigned value:

The quantification will be represented by the robust mean of the participants' results and its corresponding uncertainty. The evaluation of samples as suitable/unsuitable will be decided by a consensus of 75% of the participants. If this consensus is not reached, the assigned value will be "Inconclusive" and the parameter will not be evaluable.

Scores and evaluation:

Each pass/fail result that matches the assigned value is considered correct and receives 0 points, while each non-matching value will score 1 point.

For a result to be considered correct, its z-value must be within the acceptance interval.

Scores:

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

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points for any given parameter and to have submitted complete results for 5 of the samples. All participating laboratories will be able to download their certificate of competence for residual leukocyte analysis within 6 weeks of the end of the annual program.

IC-48: Phenotype, diagnosis and minimal residual disease (MRD) in onco-hematopoietic pathology

Purpose:

To evaluate participants' performance in diagnosing immunological and hematopoietic diseases based on phenotypic and clinical data. To evaluate participants' performance in determining cellular phenotypes in neoplasms of hematopoietic and lymphoid organs. To evaluate participants' performance in detecting residual neoplastic cells (of known phenotype) in immunological and hematopoietic diseases.

Sample distribution:

Six samples will be evaluated annually and distributed in three shipments of two samples each. The volume of the aliquots will depend on the cellularity of the samples and will be determined by the center that recruits the patients.

Results Report:

a) The general and precise diagnosis for the sample will be reported, based on the WHO classification in its 5th edition (Annex I: Diagnosis of hematological malignancies). In the case of multidrug-resistant organisms (MDROs), only the presence/absence of MDROs (and percentage if present) will be indicated.

b) Lineage, size, complexity and stage (only in leukemias, not in MRD).

c) Percentage of pathological population relative to the total leukocytes in the sample

d) Number of events collected (exclusively in EMR, the Committee recommends studying at least 106 events)

e) Immunophenotype (free text that will be included in the individual laboratory report and may be assessed)

f) Panel of antigens in pathological cells (Annex II). This panel of markers, predefined according to the type of pathology under study, will be reviewed annually by the Cellular Immunity Steering Committee. In cases of multidrug-resistant diseases (MDRD), only the markers indicated for diagnosis will be recorded. Up to two pathological cell populations may be characterized; any third or subsequent populations will be included in the observations section.

The report will be sent to GECLID within 2 weeks of receiving each shipment.

Determining the assigned value. Scoring and evaluation:

a. Quantitative parameters:

The quantification (%) will be represented by the robust mean of the participants' results and their corresponding uncertainty.

Scores, %:

- z ∈ (-2, 2) correct result (0 points)
- z ∈ (-3, -2] ∪ [2, 3) Warning signal: questionable result (1 point)

- z ∈ (-, -3]U[3,) action signal: incorrect result (2 points)∞∞

b. Qualitative parameters:

The diagnostic value will be validated by the Leukemia/Lymphoma and MRSD Specialist Advisor, using the value closest to that provided by the Collaborating Center supplying the samples, consistent with the consensus of participating laboratories and experts, and included in the aforementioned list (WHO 2022). The Leukemia/Lymphoma and MRSD Specialist Advisor may decide to modify this value and/or request that the decision be made by expert consensus (defined as laboratories with the fewest errors in previous rounds, as outlined in ISO 17043). All other acceptable diagnoses will be designated as accepted diagnoses and will be determined by the Expert Advisor. If sufficient consensus (75%) is not reached, the diagnosis will be recorded as "Inconclusive" and will not be evaluated. The result corresponding to the expert laboratory consensus will also be included; expert laboratories are defined as those that have accumulated less than two errors during the previous year. The results will be scored according to the following criteria:

For a result to be considered correct, it must match the assigned value (consensus):

- Report a value that matches the assigned one (0 points)
- Reporting a value other than the one assigned or failing to report a parameter:
  - In the case of a parameter NOT necessary (the Cellular Immunity Steering Committee will determine which parameters are dispensable in each case) for the diagnosis or prognosis of the pathology of the sample or in the case of parameters assigned as Inconclusive, which will not imply penalties in any case (0 points).
  - In the case of an essential parameter, that is, one that affects the definitive diagnosis of the sample (the Cellular Immunity Steering Committee will determine which parameters are essential in each case) (1 point).

In addition to the scores, the individual reports will include the personalized notes indicated for each participant by the Specialist Advisor in Leukemias/Lymphomas and MRD whenever it is considered appropriate and especially in cases where an erroneous diagnosis has been reported.

c. Diagnosis:

Diagnostic compatibility will be assigned to each sample by consensus of at least 75% of the participating laboratories. If this consensus is not reached, the Specialist Advisor for Leukemias/Lymphomas and MRSD and/or the opinion of the Cellular Immunity Steering Committee will be consulted. In case of disagreement with the consensus value, the results will be scored according to the following criteria:

- Report the consensus diagnostic compatibility or a broader generic one (in bold in the list above) that includes the assigned diagnosis and does not affect the therapeutic approach and/or the prognosis of the patient (0 points).
- Report a diagnosis different from the assigned diagnosis and different from its broader generic one, but which does not affect the therapeutic approach and/or the prognosis of the patient (0.5 points).
- Reporting a diagnosis different from the assigned diagnosis that clearly affects the therapeutic approach and/or the prognosis of the patient (1 point).

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points in any one parameter and to have submitted complete results for 4 of the samples. All participating laboratories will be able to download their certificate of competence for the study and diagnosis of leukemias/lymphomas within 6 weeks of the end of the annual period.

**The IC-48 Leukemia/Lymphoma and MRD Immunophenotyping Scheme is not included in the scope of the SIC-SEI agreement, although members of either society may participate in it under the same conditions as in the other schemes.*

IC-5: Lymphocyte Function

Purpose:

To evaluate the performance of participants in the study of lymphocyte response to mitogens, of particular importance in patients with primary immunodeficiencies or undergoing immunosuppressive treatments.

Sample distribution:

Six samples will be evaluated annually, distributed in two shipments of three samples each. The approximate volume of the aliquots is 2 mL.

Results Report:

Each laboratory will report, using the Telematic Results Form, the results obtained for proliferative response: normal, elevated or decreased in response to PHA (Phytohemagglutinin A), PWM (Pokeweed Mitogen) and a negative control, or for ATP production by CD4+ lymphocytes in response to PHA.

The results will be reported to GECLID within 2 weeks of receiving the samples.

Determining the assigned value. Scoring and evaluation:

a. Quantitative parameters:

The quantification (%) will be represented by the robust mean of the participants' results and their corresponding uncertainty.

Scores, %:

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

b. Qualitative parameters:

The value assigned to the qualitative parameters of this scheme will be determined in each case by consensus of at least 75% of the participating laboratories. If this consensus is not reached, the assigned value will be "Inconclusive" and the parameter will not be evaluated. The results will be scored according to the following criteria:

For a result to be considered correct, it must match the assigned value (consensus):

- Report a proliferation value matching the assigned one (0 points)
- Report a proliferation value different from the one assigned (1 point)

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points in any one parameter and to have submitted complete results for 5 of the samples. All participating laboratories will be able to download their certificate of competence for the study of innate function within 6 weeks of the end of the annual exercise.

IC-6: Innate function

Purpose:

Evaluate the performance of participants in the functional study of innate immunity, by determining the phagocytic and oxidative capacity (burst test) of neutrophils and monocytes from blood samples.

Sample distribution:

Six samples will be evaluated annually, distributed in two shipments of three samples each. The approximate volume of the aliquots is 1 mL.

Results Report:

Each laboratory will report the results obtained for phagocytosis and burst in both monocytes and granulocytes using the Telematic Results Form.

	Phagocytosis	Burst
MONOCYTES	**normal/elevated/decreased phagocytosis**	**Normal/high/decreased burst**
	Count	Count
	% in unstimulated cells	% in unstimulated cells
	% in cells stimulated with E. coli	% in cells stimulated with E. coli
GRANULOCYTES	**normal/elevated/decreased phagocytosis**	**Normal/high/decreased burst**
	Count	Count
	% in unstimulated cells	% in unstimulated cells
	% in cells stimulated with E. coli	% in cells stimulated with E. coli

The results will be reported to GECLID within 2 weeks of receiving the samples.

Determining the assigned value. Scores and evaluation:

a. Quantitative parameters:

The quantification (%) will be represented by the robust mean of the participants' results and their corresponding uncertainty.

Scores, %:

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

b. Qualitative parameters:

The value assigned to the qualitative parameters of this scheme will be determined in each case by consensus of at least 75% of the participating laboratories. If this consensus is not reached, the assigned value will be “Inconclusive” and the parameter will not be evaluated. The results will be scored according to the following criteria:

For a result to be considered correct, it must match the assigned value (consensus):

- Report a phage/burst value that matches the assigned one (0 points)
- Report a phage/burst value different from the one assigned (1 point)

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points in any one parameter and to have submitted complete results for 5 of the samples. All participating laboratories will be able to download their certificate of competence for the study of innate function within 6 weeks of the end of the annual exercise.

IC-7: Molecular-Leukemia

Purpose:

Evaluate the performance of participants in the determination by molecular biology techniques of markers in immunological and hematopoietic diseases.

Sample distribution:

Six samples will be evaluated annually and distributed in three shipments of two samples each. The volume of the aliquots will depend on the cellularity of the samples and will be determined by the center that recruits the patients.

Results Report:

The results obtained will be collected for:

- T clonality (mono, poly or oligoclonal, region and size of monoclonal peak)
- Clonality B (mono, poly or oligoclonal, region and size of monoclonal peak)
- BCR/ABL:
  - p210: presence/absence of the translocation, number of copies (this will be collected along with the number of copies of the ABL or GUS control gene according to the routine of each laboratory, although this data will not be evaluable), % BCR-ABL p210: (Number of BCR-ABL p210 copies / Number of Control copies x 100), International Score (IS) (% BCR-ABL x correction factor, the correction factor used by the laboratory will be collected along with this data, which will never be evaluable) qualitative (type of transcript) optional
  - p190: mandatory qualitative, optional quantification presence/absence of the translocation, number of copies (will be collected together with the data on the number of copies of the ABL or GUS control gene according to the routine of each laboratory, although this data will not be evaluable), % BCR-ABL p190: (Number of BCR-ABL p190 copies / Number of Control copies x 100)
- PML-RARA: mandatory qualitative, optional quantification presence/absence of the translocation, number of copies (will be collected together with the data on the number of copies of the ABL or GUS control gene according to the routine of each laboratory, although this data will not be evaluable), % PML-RARA: (Number of PML-RARA copies / Number of Control copies x 100)
- FLT3:
  - ITD: presence/absence and ratio
  - TKD: presence/absence and ratio
- IgH and TCR rearrangement: evaluation (Polyclonal, Monoclonal or Oligoclonal); description of monoclonal peaks (affected IgH or TCR region, and peak size in each affected region)
- Mutations in the calreticulin gene (CALR): Type 1 (52-bp deletion; c.1092_1143del)/ Type 2 (5-bp insertion; c.1154_1155insTTGTC/Other: specify type 3-36)/none
- Mutations in MPL (myeloproliferative leukemia protein, CD110): Ser505Asn-S505N/exon 10-W515KL/Other
- Mutations in the JAK2 V617F gene and exon 12: location, type (insertion/deletion, substitution); ratio
- NPM1

The report will be sent to GECLID within 4 weeks after receiving each shipment.

Determining the assigned value. Scoring and evaluation:

a. Quantitative parameters:

The quantification (%) will be represented by the robust mean of the participants' results and their corresponding uncertainty.

Scores, %:

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

b. Qualitative parameters:

The value assigned to the qualitative parameters of this scheme will be determined in each case by consensus of at least 75% of the participating laboratories. If this consensus is not reached, the assigned value will be "Inconclusive" and the parameter will not be evaluated. The results will be scored according to the following criteria:

For a result to be considered correct, it must match the assigned value (consensus):

- Report a value/intensity that matches the assigned one (0 points)
- Reporting a value different from the one assigned (1 point)

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points in any one parameter and to have submitted complete results for 4 of the samples. All participating laboratories will be able to download their certificate of competence for the study and diagnosis of leukemias/lymphomas within 6 weeks of the end of the annual period.

Determining the assigned value for qualitative parameters:

The value assigned to the qualitative parameters of this scheme will be determined in each case by consensus of at least 75% of the participating laboratories. The results will be scored according to the following criteria:

For a result to be considered correct, it must match the assigned value (consensus):

- Report a presence/absence matching the value assigned for the sample (0 points)
- Report a presence/absence different from the value assigned for the sample (1 point)

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points in any one parameter and to have submitted complete results for 4 of the samples. All participating laboratories will be able to download their certificate of competence for the study and diagnosis of leukemia/lymphoma within 6 weeks of the end of the annual period.

IC-9: Monitoring of anti-CD20 therapies

Purpose:

To evaluate the performance of participants in the detection and analysis of high sensitivity (below 1% to 0.01%) of B lymphocyte populations in patients treated with anti-CD20 biological drugs (rituximab).

Sample distribution:

Six samples will be evaluated annually (generally peripheral blood anticoagulated with EDTA-K3) and will be distributed in two shipments of three samples each. The approximate volume of the aliquots is 300 µL. Participants may request additional aliquots by indicating this on their registration form or by emailing the program coordinator.

Results Report:

Results will be recorded of percentage of CD19+CD20+ B lymphocytes, memory B lymphocytes (CD19+CD27+), and plasmablasts (optional). Reporting the number of events collected is mandatory (although not evaluable), as is reporting the percentage of CD19+ and CD20+ B lymphocytes. Physicians may report the remaining percentages. Each laboratory will report its results using the form at https://www.geclid.es/.

The percentages of CD19+ and CD20+ B lymphocytes will be relative to the total lymphocytes, while those of memory and plasmablasts will be relative to the total B lymphocytes. Relating percentages to other parameters may result in penalties. Results will be reported to GECLID within 2 weeks of sample receipt.

Determining the assigned value:

The quantification will be represented by the robust mean of the participants' results and its corresponding uncertainty.

Scores and Evaluation:

For a result to be considered correct, its z-value must be within the acceptance interval.

Scores:

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

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points for any given parameter and to have submitted complete results for 5 of the samples. All participating laboratories will be able to download their certificate of competence for the determination of lymphocyte populations within 6 weeks of the end of the annual period.

IC-10: PD-1 Lymphocytes

Purpose:

Evaluate the performance of participants in the detection and analysis of lymphocyte populations of PD1-positive lymphocytes in solid tumors %PD1+CD8+ or %PD1CD4+

Sample distribution:

Six samples will be evaluated annually and distributed in two shipments of three samples each. The approximate volume of each aliquot is 300 µL. Participants may request additional aliquots by indicating this on their registration form or by emailing the program coordinator.

Results Report:

Lymphocyte percentage results will be collectedPD1+CD8+andPD1+CD4+Reporting the number of events collected is mandatory (although it is not evaluable). Each laboratory will report its results using the form at https://www.geclid.es/.

The percentages of lymphocytes%PD1+CD8+ or %PD1CD4+These percentages will refer to the total lymphocyte count. Using other parameters may result in penalties. Results will be reported to GECLID within 2 weeks of sample receipt.

Determining the assigned value:

The quantification will be represented by the robust mean of the participants' results and its corresponding uncertainty.

Scores and Evaluation:

For a result to be considered correct, its z-value must be within the acceptance interval.

Scores:

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

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points for any given parameter and to have submitted complete results for 5 of the samples. All participating laboratories will be able to download their certificate of competence for the determination of lymphocyte populations within 6 weeks of the end of the annual period.

IC-11: Repertoire T

Purpose:

Evaluate the performance of participants in the detection and analysis of T subfamilies

Sample distribution:

Six samples will be evaluated annually and distributed in two shipments of three samples each. The approximate volume of each aliquot is 300 µL. Participants may request additional aliquots by indicating this on their registration form or by emailing the program coordinator.

Results Report:

Results will be recorded of percentage of lymphocyte subfamilies T. Reporting the number of events collected is mandatory (although it is not evaluable). Each laboratory will report its results using the form at https://www.geclid.es/.

Regarding the percentages of the different subfamilies, these percentages will refer to the total number of T lymphocytes. Referring percentages to other parameters may result in penalties. Results will be reported to GECLID within 2 weeks of receiving the samples.

Determining the assigned value:

The quantification will be represented by the robust mean of the participants' results and its corresponding uncertainty.

Scores and Evaluation:

For a result to be considered correct, its z-value must be within the acceptance interval.

Scores:

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

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points for any given parameter and to have submitted complete results for 5 of the samples. All participating laboratories will be able to download their certificate of competence for the determination of lymphocyte populations within 6 weeks of the end of the annual period.

IC-12: Advanced T and B Phenotype

Purpose:

Evaluate the performance of participants in the detection and analysis of naïve, effector, regulatory, memory, activated, plasmablasts, and transitional T and B lymphocytes

Sample distribution:

Four samples will be evaluated annually and distributed in two shipments of two samples each. The approximate volume of each aliquot is 400 µL. Participants may request additional aliquots by indicating this on their registration form or by emailing the program coordinator.

Results Report:

All B populations on B CD19+

Population	Recommended markers
B naïve*	CD19+, CD38-,CD27-, IgM+, IgD+ High
B memory switched*	CD19+, CD27+, CD21+ IgM-, IgD-
CD21LOW	CD19+, CD21low, CD38low, CD27-
B marginal like	CD19+, CD27+, IgM++, IgD+
Plasmablasts	CD19+low, CD21+, CD38++, CD27+
Transitional B	CD19+, CD38++, IgM++, CD27-,CD21+

For T cell subpopulations, the focus would be on CD4 or CD8 cells as appropriate; it is recommended to exclude gamma deltas.

Population	Recommended markers
CD4 Main Memory*	CD3+, CD4+, CCR7+, CD45RA-
CD4 naïve*	CD3+, CD4+, CCR7+, CD45RA+
CD4 effector memory*	CD3+, CD4+, CCR7-, CD45RA-
CD4 effectors*	CD3+, CD4+, CCR7-, CD45RA+
Activated CD4 T lymphocytes	CD3+, CD4+, CD25+, HLA DR+
TREG lymphocytes	CD3+, CD4+, CD127-, CD25++
TREG memory	CD3+, CD4+, CD127-, CD25++, CDRA-
TREG naïve	CD3+, CD4+, CD127-, CD25++, CDRA+
Th1 (out of total CD4)	CD3+, CD4+, CXCR3+, CCR6-
Th2 (out of total CD4)	CD3+, CD4+, CXCR3-, CCR6-
Th17 so (on total CD4)	CD3+, CD4+, CXCR3-, CCR6+
CD8 main memory*	CD3+, CD8+, CCR7+, CD45RA-
CD8 naïve*	CD3+, CD8+, CCR7+, CD45RA+
CD8 effector memory*	CD3+, CD8+, CCR7-, CD45RA-
CD8 effectors*	CD3+, CD8+, CCR7-, CD45RA+
CD4- CD8- TCR alpha-beta T lymphocytes	CD3+, CD4-, CD8-, TCRalpha/beta+

Reporting the number of events collected (although not evaluable) and the antibody panel used is mandatory. Each laboratory will report its results using the form at https://www.geclid.es/.

Percentages will refer to the total number of lymphocytes of their class (CD4+, CD8+, B cells). Referring percentages to other parameters may result in penalties. Results will be reported to GECLID within 2 weeks of receiving the samples.

Determining the assigned value:

The quantification will be represented by the robust mean of the participants' results and its corresponding uncertainty.

Scores and Evaluation:

For a result to be considered correct, its z-value must be within the acceptance interval.

Scores:

- $z \in (-2, 2)$ correct result (0 points)

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

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points for any given parameter and to have submitted complete results for 5 of the samples. All participating laboratories will be able to download their certificate of competence for the determination of lymphocyte populations within 6 weeks of the end of the annual period.

IC-13: Ploidy and Cell Cycle

Purpose:

Evaluate the performance of participants in the assessment of aneuploidy and cellular DNA content by flow cytometry.

Sample distribution:

Two samples will be evaluated annually and distributed in two shipments of one sample each. The approximate volume of the aliquots is 0.5 mL.

Results Report:

Each laboratory will report the results obtained for ploidy (diploid, hypodiploid, hyperdiploid) and cell cycle (% of cells in G1, G2, and S) using the form at https://www.geclid.es/ . The results will be reported to GECLID within 2 weeks of receiving the samples.

Determining the assigned value. Scoring and evaluation:

c. Quantitative parameters:

The quantification (%) will be represented by the robust mean of the participants' results and their corresponding uncertainty.

Scores, %:

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

d. Qualitative parameters:

The value assigned to the qualitative parameters of this scheme will be determined in each case by consensus of at least 75% of the participating laboratories. If this consensus is not reached, the assigned value will be "Inconclusive" and the parameter will not be evaluated. The results will be scored according to the following criteria:

For a result to be considered correct, it must match the assigned value (consensus):

- Report a ploidy value matching the assigned one (0 points)
- Report a ploidy value different from the one assigned (1 point)

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points for any one parameter and to have submitted complete results for both samples. All participating laboratories will be able to download their certificate of competence for ploidy testing no later than 6 weeks after the end of the annual exercise.

IC-14: MLPA-LLA

Purpose:

Evaluate the performance of participants in detecting abnormal copy number changes (insertions or deletions) of genomic sequences using multiple ligation-dependent probe amplification.

Sample distribution:

Two samples will be evaluated annually and distributed in two shipments of one sample each. The approximate volume of the aliquots is 0.5 mL.

Results Report:

Each laboratory will report, via the form at https://www.geclid.es/, the results obtained for copy number variations (CNVs) caused by deletions or duplications of genes involved in the differentiation and cell cycle control of B lymphocytes (EBF1, CDKN2A/B, PAX5, ETV6, BTG1, and RB1) and in the PAR1 region, using MLPA analysis of genomic DNA (extracted from blood or bone marrow). The results to be reported for each gene will be:

- No change in the number of copies
- Heterozygous or homozygous deletion
- Heterozygous or homozygous duplication
- Method and manufacturer used.

The results will be reported to GECLID within 2 weeks of receiving the samples.

Determining the assigned value. Scoring and evaluation:

e. Quantitative parameters:

The quantification (%) will be represented by the robust mean of the participants' results and their corresponding uncertainty.

Scores, %:

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

f. Qualitative parameters:

The value assigned to the qualitative parameters of this scheme will be determined in each case by consensus of at least 75% of the participating laboratories. If this consensus is not reached, the assigned value will be “Inconclusive” and the parameter will not be evaluated. The results will be scored according to the following criteria:

For a result to be considered correct, it must match the assigned value (consensus):

- Report a variation value that matches the assigned value (0 points)
- Report a variation value different from the one assigned (1 point)

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points for any given parameter and to have submitted complete results for both samples. All participating laboratories will be able to download their certificate of competence for the MLPA study within 6 weeks of the end of the annual exercise.

IC-15: BAL Populations

Purpose:

To evaluate the participants' performance in the detection and analysis of cell populations in bronchoalveolar lavage (BAL): total lymphocytes, CD4 T lymphocytes, CD8 T lymphocytes, CD4/CD8 ratio, neutrophils, alveolar macrophages, eosinophils, and CD1a+ Langerhans cells on BAL samples preserved with Transfix. Optionally, the percentages of B lymphocytes (CD19+ and/or CD20+), CD56+ NK cells, and CD117++ mast cells will be reported.

Sample distribution:

Three samples will be evaluated annually, distributed in three shipments of one sample each. The approximate volume of the aliquots will be 0.5 mL.

Results Report:

Percentages (referring to the total CD45+ cells) and absolute count (optional) of populations: total lymphocytes, CD4+ T lymphocytes, CD8+ T lymphocytes, CD4/CD8 ratio, B lymphocytes (optional), NK cells (optional), neutrophils, alveolar macrophages, eosinophils, CD1a+ Langerhans cells, and mast cells (optional). Reporting the number of events collected (although not evaluable) and the antibody panel used is mandatory. Each laboratory will report its results using the form at https://www.geclid.es/ .

Referring percentages to other parameters may result in penalties. Results will be reported to GECLID within 2 weeks of receiving the samples.

Determining the assigned value:

The quantification will be represented by the robust mean of the participants' results and its corresponding uncertainty.

Scores and Evaluation:

For a result to be considered correct, its z-value must be within the acceptance interval.

Scores:

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

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To obtain a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points for any one parameter and to have submitted complete results for 5 of the samples. All participating laboratories will be able to download their certificate of competence for the determination of lymphocyte populations in BAL within a period of no more than 6 weeks from the end of the annual exercise.

IC-17: Monitoring of CAR-T therapies

Purpose:

To evaluate the performance of participants in the monitoring of CAR-T cells (Chimeric Antigen Receptor) and B lymphocytes in patients treated with this advanced therapy.

Sample distribution:

Two annual samples (of peripheral blood anticoagulated with EDTA-K3) will be evaluated and distributed in two shipments of one sample each. The approximate volume of the aliquots is 500 µL. Participants may request additional aliquots by indicating this on their registration form or by emailing the program coordinator.

Results Report:

Results will be recorded of percentage of leukocytes (CD45+), T lymphocytes (CD3, CD4, CD8), and CAR (Tγδ,B and NK optionally), with the number of events collected being mandatory to report (although it is not

evaluable), and the remaining percentages optional. Each laboratory will report its results using the form at https://www.geclid.es/ .

Percentages will refer to the population indicated in each case. Referring percentages to other parameters may result in penalties. Results will be reported to GECLID within 2 weeks of receiving the samples.

Determining the assigned value:

The quantification will be represented by the robust mean of the participants' results and its corresponding uncertainty.

Scores and Evaluation:

For a result to be considered correct, its z-value must be within the acceptance interval.

Scores:

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

The accumulation of 2 or more points in the same parameter in two consecutive rounds shows the occurrence of anomalies that should be investigated and corrected by the laboratory (2).

To receive a satisfactory report at the end of the (annual) program, it will be necessary to have obtained 2 or less points for any one parameter and to have submitted complete results for 5 of the samples. All participating laboratories will be able to download their CAR monitoring competency certificate no later than 6 weeks after the end of the annual period.

Annex I: Diagnosis of hematopoietic neoplasms based on the classification proposed by the WHO in its 5th edition

Diagnosis
Myeloid or lymphoid neoplasms associated with eosinophilia and abnormalities in PDGFRA, PDGFRB, or FGFR1 receptors (NER) transformed into an acute process
Myelodysplastic or myeloproliferative syndromes
Acute myeloid leukemia and related neoplasms (AML)
blastic plasmacytoid dendritic cell neoplasm
Acute leukemias of ambiguous lineage (LALA)
Lymphoblastic leukemia T-cell lymphoma (LLT)
T-cell and NK-cell (LTNK) neoplasms
Lymphoblastic leukemia B lymphoma (LLB)
Lymphoid neoplasms
B-cell precursor neoplasm
Mature B-cell neoplasm
Plasma cell neoplasia and other paraprotein diseases
T-cell precursor neoplasm
Mature T or NK cell neoplasm
Myeloid neoplasms
Myelodysplastic neoplasms
Myelodysplastic/myeloproliferative neoplasms
Acute myeloid leukemia (defined by maturation)
Acute leukemia of ambiguous lineage (LALA) defined by immunophenotype
Plasmacytoid dendritic cell neoplasm

Family
Secondary myeloid neoplasms
Myeloproliferative neoplasms (MPN)
NER: Myeloid/lymphoid neoplasms with eosinophilia and defining genetic rearrangement
NER: Myeloid precursor lesions
MDS: Myelodysplastic neoplasms (MD, formerly known as myelodysplastic syndrome, MDS)
AML: Acute myeloid leukemia (AML)
Mastocytosis
LALA: Juvenile myelomonocytic leukemia (JMML)
LALA: Acute leukemias of mixed or ambiguous lineage
LALA: Tumor-like lesions with a predominance of T cells
LLT: T cell precursor neoplasms
LTNK: Mature T-cell and NK cell neoplasms
LLB: Tumor-like lesions with a predominance of B cells
LLB: Precursor B-cell neoplasms (B-lymphoblastic leukemia/lymphoma (B-LBL/L) with defined genetic alterations and B-LBL/L, NOS)
LLB: Plasma cell neoplasms (PCN) and other paraprotein diseases
NPB: B lymphoblastic leukemia/lymphoma
Neo B: Monoclonal lymphocytosis B
Neo B: B-CLL/lymphocytic B-NHL
Neo B: Hairy cell leukemia
Neo B: Marginal NHL-B

Neo B: Lymphoplasmacytic lymphoma

Neo B: Follicular lymphoma

Neo B: Mantle lymphoma

Neo B: Transformation of an indolent B lymphoma

Neo B: Large B cell lymphoma

Neo B: Burkitt lymphoma

Neo B: Lymphoid proliferations and B lymphomas associated with KSHV/HHV-8

Neo B: Hodgkin lymphoma

Monoclonal gammopathy of undetermined significance

Multiple Myeloma

TPN: T lymphoblastic leukemia/lymphoma NOS

NPT: Early T-cell precursor lymphoblastic leukemia/lymphoma

Neo TNK: T-cell prolymphocytic leukemia

Neo TNK: T-cell large granular lymphocyte leukemia

Neo TNK: NK large granular lymphocyte leukemia

Neo TNK: Adult T leukemia/lymphoma

Neo TNK: Sézary Syndrome

Neo TNK: Aggressive NK cell leukemia

Neo TNK: Hepatosplenic T lymphoma

Neo TNK: Anaplastic large cell lymphoma

Neo TNK: T follicular helper nodal lymphoma (angioimmunoblastic/follicular type)

Myeloproliferative neoplasms

LMM: Chronic myelomonocytic leukemia

LAM with minimal differentiation

LAM without maturation

LAM with maturation

LAM: Acute basophilic leukemia

LAM: Acute myelomonocytic leukemia

LAM: Acute monocytic leukemia

LAM: Acute erythroid leukemia

LAM: Acute megakaryoblastic leukemia

LALA: Acute leukemia of mixed B/myeloid phenotype

LALA: Acute leukemia of mixed T/myeloid phenotype

LALA: Acute leukemia of mixed phenotype, other variants

LALA: Acute leukemia of ambiguous lineage, not otherwise specified

LALA: Acute undifferentiated leukemia

Annex II: Panel of markers for the diagnosis of oncohematopoietic neoplasms

CD1a	CD11b	CD24	CD36	CD49d	CD65	CD105	CXCR5	λ in cytoplasm
CD2	CD11c	CD25	CD38	CD52	CD66c	CD117	NG2	TCR αβ
CD3 surface	CD13	CD26	CD39	CD55	CD71	CD123	cBCL2	TCR γδ
CD3 cytoplasm	CD14	CD27	CD41	CD56	cCD79a	CD138	LAIR1 (CD305)	cMPO
CD4	CD15	CD28	CD42b	CD57	CD79b	CD200	FMC7	cPerforin
CD5	CD16	CD30	CD43	CD58	CD81	CD203c	nuTdT	cGranzyme
CD7	CD19	CD31	CD44	CD59	CD94	CD235a	cIgM	β2 microglobulin
CD8	CD20	CD33	CD45	CD61	CD95	CD279	κ on surface	
CD9	CD22	CD34	CD45RA	CD62L	CD99	CD300e	κ in cytoplasm	
CD10	CD23	CD35	CD45RO	CD64	CD103	CCR7	λ on surface	

CRITERIA/REQUIREMENTS FOR PARTICIPATION

Only one registration per laboratory will be allowed in the Subprogram for the purpose of determining the assigned values.
For all schemes, laboratories participating in this subprogram must include their own positive and negative controls.
For all schemes, participants must note the method used in the space provided for this purpose on the results submission form.

LABORATORY RESPONSIBLE FOR DISTRIBUTIONS

The laboratory that will be responsible for the handling and distribution of samples and for evaluating the test results is the Immunology Laboratory of the Hemotherapy and Hemodonation Center of Castilla y León in Valladolid.

SAMPLES, SPECIMENS OR ITEMS

Nature of the samples

The samples in this subprogram are always of human origin, with minimal manipulation, so that they are as similar as possible to those in the usual practice of diagnostic laboratories. The methods used in the preparation and distribution of samples have been shown (SEI Workshops) to be adequate to guarantee their homogeneity and stability under the conditions detailed.
The samples are mostly peripheral blood (EDTA blood, HepNa blood, buffy coats). They will be divided into aliquots of different volumes depending on the test.burn the one that corresponds. All handling will be carried out under sterile conditions. Samples will be kept and shipped at room temperature within 36 hours of collection. They must be used within 24 hours of receipt; after this time, their viability and stability cannot be guaranteed. Stem cell analysis will use cells obtained from umbilical cords.

All samples, regardless of type, will have been tested for infectious agents before submission, ensuring that laboratories are informed upon collection if any positive serologies are found. Should such circumstances arise, GECLID will withdraw the sample from the interlaboratory comparison exercise and replace it with another. In general, even if all serologies on the proposed panel are negative, all samples should be handled, as in clinical practice, as potentially infectious.

Types of samples

DONOR SAMPLES: presumably healthy, but which are still analyzed to rule out infectious pathologies.

PATIENT SAMPLES Through GECLID's collaborating centers, peripheral blood, cord blood, and bone marrow (where applicable) will be collected from patients for various programs. The samples distributed within GECLID's subprograms and programs will be obtained from different blood banks and clinical services throughout Spain, in accordance with current legislation.

DESIGN SAMPLES: For certain schemes, samples will be prepared with specific manipulations that allow emulating pathologies.

Obtaining

Most of the samples included in this scheme come from biobanks. However, laboratories participating in the offered subprograms and schemes may negotiate with GECLID the inclusion of local samples (serum, blood) from their patients in any of the quality schemes (especially when diagnoses are infrequent or relevant), in accordance with the Collaborator Manual. For this inclusion, they must provide all the data that allows for sample traceability, safety (negative serologies for applicable infectious agents), and compliance with applicable regulations (Sample Transfer Agreement and Informed Consent of the corresponding sample donors), as well as the associated clinical information.

Sample collection will be carried out according to the protocol of the Collaborating centers/Biobanks after the corresponding informed consent of the donor.

Prosecution

The samples will be processed under appropriate environmental conditions to preserve their integrity (handling at room temperature and in a laminar flow hood when necessary).

Transport

All samples will be distributed in suitable packaging following IATA regulations and accompanied by their documentation which will include at least: the sample number, additives and/or preservatives it contains and the analyses that are expected to be carried out on each sample by the participating laboratories.

All samples included in the quality schemes will have a documented traceability system: origin, serology, personnel who handled and packaged it, date of extraction and shipment, etc.

GECLID will retain a portion of each batch of samples for at least one year, so that laboratories that request it can acquire extra volumes (paying the corresponding costs) and additional tests can be re-analyzed if necessary.

STATISTICAL METHODS AND SCORING SYSTEMS

The criteria are detailed in each scheme. Participants are reminded that the accumulation of 2 or more points for the same parameter in two consecutive rounds indicates anomalies that should be investigated and corrected by the laboratory (2). The criteria for scheme scoring will be reviewed annually by GECLID based on current quality standards for interlaboratory comparison providers (4) and ENAC recommendations.

INFORMATION

The reports will be comprehensive and clear, including both numerical data and graphs to facilitate the understanding and interpretation of the results. Follow-up data will also be included when available. The use of combined scores for multiple schemes will be avoided (4). The following is issued for each scheme:

- Global sample report: This will include a descriptive study of all collected data and conclusions. Stratified analyses by method will be included whenever there are at least 10 participants.
- Results of individual laboratory participation and score obtained in each of the schemes
- LEM Report (Laboratories, equipment and methods): collecting the frequencies of participation by region, methods and reagents used

Each participating laboratory will be identified in these reports solely by its unique code. Laboratories will not be ranked by performance under any circumstances. These reports will be issued/published by GECLID approximately two weeks after the close of each interlaboratory comparison round for each scheme. Laboratories that submitted their results late for any reason will have a note to that effect on the cover page of their individual report.

Laboratories will be able to download their reports for each round, as well as the annual evaluation summary in electronic format (pdf) at https: //geclid.centrodehemoterapiacyl.es This certificate will be available no later than 6 weeks after the end of the fiscal year. Laboratories that request it may obtain a certificate detailing the schemes in which they participate before the end of the fiscal year, but in this case, it will not contain scoring or evaluation data.

Participating laboratories will be responsible for ensuring that their documentation relating to the interlaboratory comparison program is and remains available to auditors or inspectors from the accreditation bodies (ENAC, etc…) that apply to them.

BASIS FOR ANNUAL PERFORMANCE EVALUATION

The annual evaluation consists of two elements:

- Number of samples reported: each scheme indicates the minimum number of samples required for a satisfactory evaluation
- Number of errors in each parameter: the accumulation of 2 points in the same parameter indicates that the laboratory must review its records and procedures and if 2 points are exceeded it must implement corrective and preventive actions

All participating laboratories will be able to download a certificate with their performance evaluation for each of the schemes in which they participated, no later than six weeks after the end of the fiscal year. Specifically, laboratories that join the Subprogram late and consequently cease to participate in any interlaboratory comparison round will be required to have submitted complete results for at least 90% of the samples received and a maximum of two points accumulated per parameter to obtain a satisfactory evaluation for the period to

which their registration applies. The laboratory may appeal its evaluation within 20 business days of receiving notification of the evaluation.

The criteria for laboratory evaluations will be reviewed annually by GECLID based on the current quality standards for interlaboratory comparison providers (1).

APPEALS AND COMPLAINTS POLICY

To file a complaint or appeal an evaluation, you must fill out the <Complaint Form> document available on the website and send it to the Program Manager by email, or through the <Appeals and Complaints: Submission Tool> web tool.

- Your complaints will be handled by the program manager at the Blood Transfusion and Donation Center
- Appeals and issues related to results, reports, or evaluations will be addressed:
    - Initially by the Immunologist in charge of the GECLID-SEI Program
    - Secondly, by the SIC-SEI Joint Steering Committee of the Cellular Immunity Subprogram
    - Thirdly and finally by the Quality Commission for Diagnostic Immunology (CCID) of the Spanish Society of Immunology
- You will be kept informed of the process of your appeal or claim, and if the outcome leads to a change in your laboratory's assessment, a new report will be prepared.

Remember that the deadline for appeals to the reports for each round of submissions will always close 1 month after the results closing date.

If the complaint relates to transcription errors in your results, you must always provide the original analysis records. Since May 2015, these types of complaints have been referred to the relevant Steering Committees.

REFERENCES

1. ISO-IEC 17043: 2023 Conformity assessment. General requirements for Proficiency Testing. International Organization for Standardization, 2023
2. ISO 13528: 2022 Statistical methods for use in proficiency testing by interlaboratory comparisons
3. Blood Transfusion Accreditation Standards 5th Ed 2022. Transfusion Accreditation Committee (cat) of the Spanish Association of Hematology and Hemotherapy
4. 5th edition of the World Health Organization Classification of Haematolymphoid Tumors, 2022