External Proficiency Testing for Immunology Labs GECLID-SEI 2020

Prospectus: Immunochemistry and Allergy subprogram

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GLOSSARY

Ig: immunoglobulin

RF: rheumatoid factor

CRP: C-reactive protein

C1q: Subcomponent C1 (first factor of the complement cascade) formed by identical polypeptide chains, each of which has a fibre end and one globular domain that recognizes the constant region of antibodies

C1 inhibitor: inhibitor of the C1-esterase, main regulator for early activation steps of the classical pathway of complement and of the activation of kallikrein, plasmin in the fibrinolytic system, the activation of factor XI in the coagulation cascade and the factor XIIa

C3: Component C3 of the complement, acting on the C3 convertases-to cause activation of this system by the classical pathway or the alternative. It is the major component of the system.

C4: Component C4 of the complement molecule of the classical pathway of complement activation, whose activation releases the C4a fragment, one of the anaphylatoxins of complement

CH50: Measurement of the activity of the classical pathway of complement, indicates the serum dilution causing 50% hemolysis in a suspension formed by a complex: sheep erythrocyte antibody.

Consensus: in all diagnostic schemes it is required that 75% of the participants agree on the results. If no consensus is established, the reference result will be taken into account

Standard deviation (σ): robust standard deviation of results calculated using the algorithm A of Appendix C STANDARD ISO 13528: 2005.

B Factor: component system exclusive of alternative complement pathway

Standard uncertainty (Ux): measure of the overall dispersion parameter calculated using the algorithm A of Appendix C STANDARD ISO 13528: 2005.

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

n= Number of laboratories reporting results of each parameter

Assigned value: attributed value to a parameter of an intercomparison item. Quantitative parameters are represented by the robust mean of the results reported by ever participant, calculated using the algorithm A in Annex C (C.3.1) ISO13528: 2015. Wherever n <5, median will be used instead.

$$x^* = \Sigma xi / p$$

So we call this Prospectus both the result is decided as correct by consensus of the participants, and the reference result.

Standard deviation (σ): robust standard deviation of results reported by participants, calculated using the algorithm A Annex C (C.3.1) ISO13528: 2015. Wherever n <5, the interquartile normalized range (C.2.3) will be used instead.

$$nIQR\ (x) = 0.7413\ (Q3\ (x) - Q1\ (x))$$

z-score: normalized distance between each reported result and the assigned value, it is used to measure the performance of each participant, according to ISO13528: 2015 (9.4) so far it indicates the position of the individual result as compared to the global

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

Acceptance range: z-score range between -2 and 2, where a numerical result is considered correct.

Correct result: result that coincides with the assigned value or whose z-score value is within the acceptance range .

Paraprotein: abnormal protein present in biological fluids, usually immunoglobulins or light chains

Reference results: It will be determined by experts' consensus, so called experts are laboratories with less than 2 errors accumulated in the 2 previous rounds.

SCHEMES

For each of the exercises of 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 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 Interlaboratory comparison receiving their scores, but without being evaluated. This feature must be reported to the Head of the Program.

Table 1: Subprogram Schemes Immunochemistry and Allergy GECLID-SEI 2020

SCHEME	PARAMETERS	Samples	Rounds	Deadline
IQ179 Serum Immunoproteins	IgG, IgA, IgM, IgE C3, C4, C1INH, Factor B * (in r2 and r5 rounds), C1q, CRP, RF	**2 sera**	**6**	**21 days**
IQ-2IgG subclasses	total IgG, IgG1, IgG2, IgG3, IgG4	**4 sera**	**2**	**4 weeks**
IQ-3 Allergen-specific IgE	Quantification of IgE antibodies against common allergens 6 (recombinant allergens included)	**2 sera**	**6**	**3 weeks**
IQ-4 Serum paraproteins	IgG, IgA, IgM, Kappa and lambda light chains (free). Characterization and quantification of the monoclonal component	**4 sera**	**2**	**4 weeks**
IQ-5 Urine paraproteins	Kappa and lambda light chains (free). Characterization and quantification of the monoclonal component	**4 urines**	**2**	**6 weeks**
IQ-6 Oligoclonal bands	Detection and characterization of monoclonal components in serum and cerebrospinal fluid	**3 serum-**	**2**	**6 weeks**
IQ-8 Complement function	CH50, capacity / activity C1 inh	**4 sera /**	**2**	**2 weeks**
IQ-14 Production of γ-IFN in response to pathogens (NEW)	**IFN-γ production in response to antigen TB**	**2 sera**	**2**	**4 weeks**
IQ-11 response to vaccination (NEW)	**pneumococcus, salmonella**	**2 sera**	**2**	**4 weeks**
IQ-15 Anti TNFa therapy monitoring	And drug levels of endogenous antibodies (adalimumab, infliximab, and etanercept).	**2 sera**	**2**	**4 weeks**
IQ-16 Soluble CD25	Concentration (IU / pg) of soluble CD25 serum	**3 sera**	**2**	**8 weeks**

Table 2: Schedule Subprogram Immunochemistry and Allergy GECLID-SEI 2020

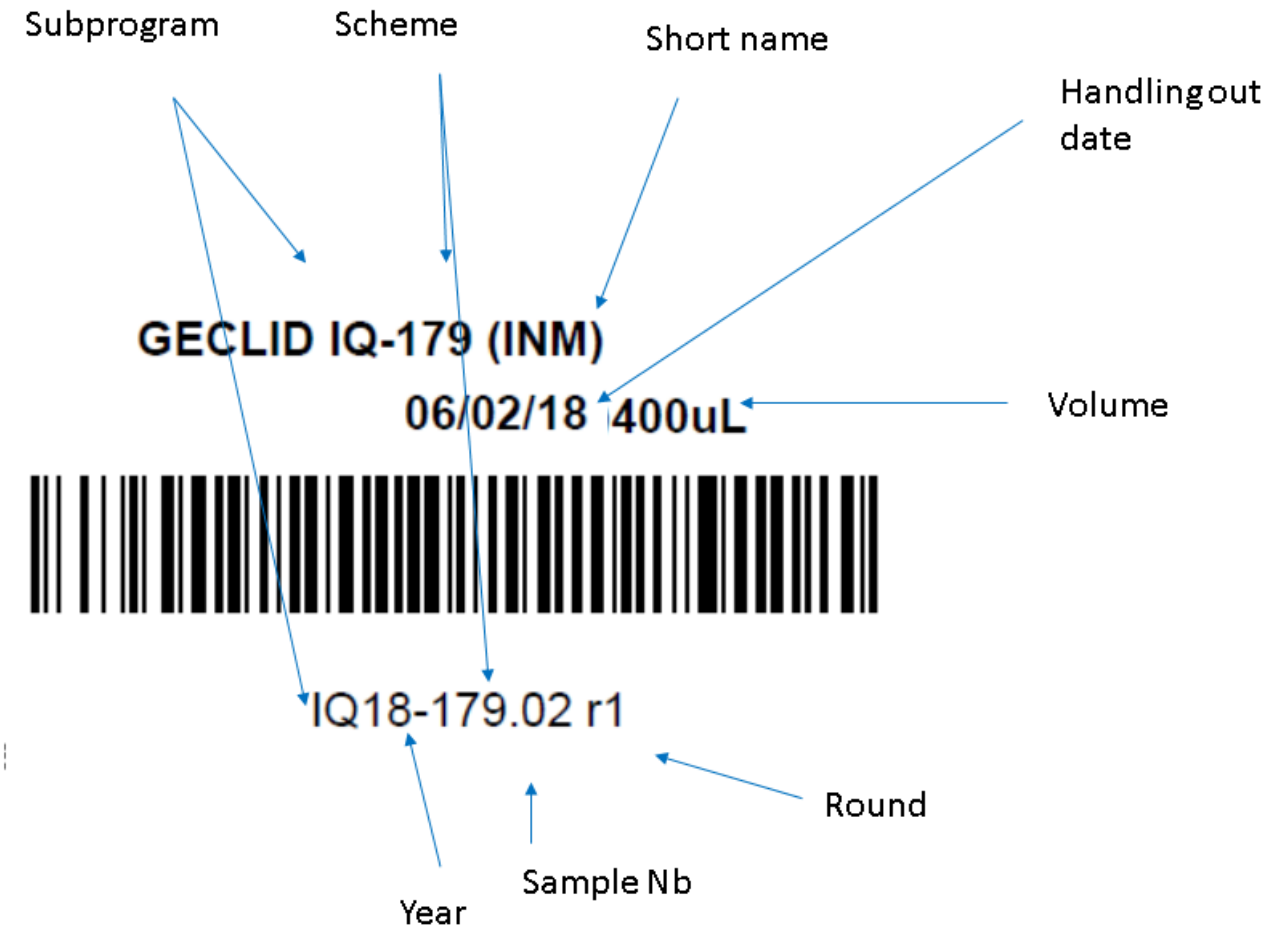
ROUND	SCHEME	
r1	IQ-11 Vaccine	02/04/2020
r1	IQ-14 γ Interferon	
r1	IQ-179 Immunoproteins (Igs, Complement, RF and CRP)	02/11/2020
r1	IQ-3 specific IgE	
r1	IQ-16 CD25 soluble	
r1	IQ-2 IgG subclasses	18/02/2020
r1	IQ-4 serum paraprotein	
r1	IQ-5 urine paraprotein	
r2	IQ-179 Immunoproteins (Igs, Complement, RF, Factor B and CRP)	03/31/2020
r2	IQ-3 specific IgE	
r1	IQ-15 anti TNFα	
r1	IQ-6 oligoclonal bands	05/05/2020
r1	IQ-8 functional Complement	
r3	IQ-179 Immunoproteins (Igs, Complement, RF and CRP)	05/19/2020
r3	IQ-3 specific IgE	
r4	IQ-179 Immunoproteins (Igs, Complement, RF and CRP)	06/16/2020
r4	IQ-3 specific IgE	
r2	IQ-11 Vaccine	09/01/2020
r2	IQ-14 Interferon γ	
r2	IQ-2 IgG subclasses	22/09/2020
r2	IQ-4 serum paraprotein	
r2	IQ-5 urine paraprotein	
r2	IQ-16 soluble CD25	
r5	IQ-179 Immunoproteins (Igs, Complement Factor B, RF and CRP)	29/09/2020
r5	IQ-3 specific IgE	
r6	IQ-179 Immunoproteins (Igs, Complement, RF and CRP)	11/17/2020
r6	IQ-3 specific IgE	
r2	IQ-6 oligoclonal bands	12/15/2020
r2	IQ-8 Complement function	

* Some dates are approximate, depending on the availability of patients

[c] Some schemes are conditioned waiting for confirmation n> 5

Sample identification

Figure 1. Identification of samples



IQ-179 Serum Immunoproteins

Purpose:

Evaluating the performance of participants in quantifying immunoglobulins, complement fractions, CRP and rheumatoid factor.

Sample distribution:

12 samples per year to be distributed in 6 shipments 2 serum samples of 400 µL will be evaluated.

Reporting results:

Within this scheme will be recorded results for:

- IgG, IgA, IgM, IgE
- C3, C4, C1INH, B Factor (r2 and r5 rounds), C1q
- CRP, RF

Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 21 days after receipt of samples.

Determination of the assigned value:

Quantification will be represented by the robust mean of results from participants and its corresponding uncertainty (ISO17043: 2010). If the number of participants were n <5, E(n) numbers may be used instead

Scoring:

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

Scores:

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

The accumulation of two or more points on a same parameter along two consecutive rounds evidences the occurrence of abnormalities 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 obtain two or less points in a same parameter and sending results of 11 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.

IQ-2: IgG subclasses

Purpose:

Evaluating the performance of participants in quantifying Immunoglobulin subclasses G.

Sample distribution:

8 samples per year to be distributed in 2 batches with four serum samples of 350 µL each will be evaluated.

Reporting results:

Within this scheme, results for total IgG, IgG1, IgG2, IgG3 and IgG4 will be recorded. Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 4 weeks after receipt of samples.

Determination of the assigned value:
Quantification will be represented by the robust mean of results from participants and its corresponding uncertainty (ISO17043: 2010).

Scoring:
For a concentration deemed correct, its z-score value must be within the acceptance range.

Scores:

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

The accumulation of two or more points on a same parameter along two consecutive rounds evidences the occurrence of abnormalities 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 obtain two or less points in a same parameter and sending results of 7 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.

IQ-3: Allergen-specific IgE

Purpose:

Evaluating the performance of participants in the detection and quantification of IgE recognizing most common allergens.

Sample distribution:

12 samples per year to be distributed in 6 shipments with 2 serum samples of 350µL each will be evaluated.

Reporting results:

Within this scheme, the quantitative results of total IgE and specific IgE recognizing allergens shall be recorded:

d1	*Dermatophagoides pteronyssinus*	g5	*Lolium perenne*
d2	*Dermatophagoides farinae*	g6	*timothy*
e1	*Cat*	g8	*Poa pratensis*
e5	*Dog*	i1	*Bee (poison)*
f1	*albumin*	i3	*Wasp (poison)*
f2	*Cow milk*	i6	*Blatella germanica* (cockroach)
f3	*cod*	k82	*latex*
f4	*wheat*	m2	*Cladosporium herbarum*
f13	*peanut*	m3	*Aspergillus fumigatus*
f14	*soy*	m6	*Alternaria alternata*
f17	*hazelnut*	p4	*anisakis*
f24	*prawns*	t3	*Betula verrucosa*
f84	*Kiwi*	t9	*Olea europea*
f95	*peach*	t11	*platanus*
F235	*lentils*	t222	*Cupressus arizonica*
F309	*chickpeas*	w6	*artemisia vulgaris*
g3	*Dactylis glomerata*	w21	*parietaria judaica*

F416 RTRI 19 Omega-5 gliadin, flour, Triticum aestivum	*f76 NBOS 4 α-lactalbumin d, milk, Bos domesticus*
F419 rPru p 1 PR-10, peach, Prunus persica	*f77 NBOS 5 β-lactoglobulin d, milk, Bos domesticus*

F421 rPru p 4 profilin, peach, Prunus persica	*F351 RPEN 1 tropomyosin, Gamba, Penaeus aztecus*
F420 rPru p3 LTP, peach, Prunus persica	*F78 NBOS D 8 Casein, Milk, Bos domesticus*
F423 rare h 2 peanut, Arachis hypogaea	*W232 Salsola kali NSAL k 1*
F424 rare h 3 Peanut, Arachis hypogaea	*T216 rBet v 2 profilin, Fir, Betula verrucosa*
F433 RTRI 14 Flour, Triticum aestivum	*t220 rBet v 4 Spruce, Betula verrucosa*
F98 nGliadin, Flour, Triticum aestivum	*t221 rBet v 2, rBet v 4 Spruce, Betula verrucosa*
g205 rPhl p 1 Grass Phleum pratense	*t225 rBet v 6 Fir, Betula verrucosa*
G213 rPhl p 1, rPhl p 5b Grass Phleum pratense	*t224 rolê e 1 Olivo, Olea europaea*
g215 rPhl p 5b Grass Phleum pratense	*t215 rBet v 1 PR-10, Spruce, Betula verrucosa*
G211 rPhl p 11 Grass Phleum pratense	*t226 nCup 1 Cupressus arizonica*
G212 rPhl p 12 profilin, Grass Phleum pratense	*Nole and 7 LTP T227, Olivo, Olea europaea*
G206 rPhl p 2 Grass Phleum pratense	*t240 rôle and 9 Olivo, Olea europaea*
G209 rPhl p 6 Grass Phleum pratense	*K221 RHEV b 8 profilin, Latex Hevea brasiliensis*
g210 rPhl p 7 Grass Phleum pratense	*M229 rAlt 1 Alternaria alternata / Alternaria tenuis*
G214 rPhl p 7, rPhl p 12 Grass Phleum pratense	*d202 rDer p 1 Mite Dermatophagoides pteronyssinus*
G208 nPhl p 4 Grass Phleum pratense	*D203 rDer p 2 Mite Dermatophagoides pteronyssinus*
F323 NGAL d 3 Conalbumin, Egg Gallus domesticus	*D205 rDer p 10 tropomyosin, Mite Dermatophagoides pteronyssinus*
F232 NGAL d 2 ovalbumin, egg, Gallus domesticus	*i209 rVes v 5 Vespula Vespula*
F233 NGAL d 1 ovomucoid, Egg Gallus domesticus	*i210 rPol d 5 Recombinant protein Antigen 5 Polistes*

Obtained results can be sent exclusively by means of the web result's form: evaluation for each allergen, class and quantification in kU / L. Data shall be recorded within 21 days after receipt of samples.

Determination of the assigned value:

Quantification will be represented by the robust mean of results from participants and its corresponding uncertainty (ISO17043: 2010).

The evaluation levels and (semi quantitative) will be determined by consensus of 75% of the participating laboratories. When this consensus were not reached, the item would be so named inconclusive and will not be evaluable.

Scoring:

For a correct result to be considered correct, it must be coincident with the Assigned value.
For a concentration deemed correct, its z-score value must be within the acceptance range.

Scores:

- Qualitative results coincident with the assigned value: correct (0 points)
- Qualitative result does is not the same as assigned value: questionable result (1 point)
- z Є (-2, 2) correct result (0 points)
- z Є (-3, -2] U [2, 3) warning: questionable result (1 point)
- z Є (-, -3] U [3,) action signal: incorrect result (2 points)

The accumulation of two or more points on a same parameter along two consecutive rounds evidences the occurrence of abnormalities 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 obtain two or less points in a same parameter and sending results of 11 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.

IQ-4: Serum paraproteins

Purpose:

Evaluating the performance of participants in the detection, characterization and quantification of paraproteins in human serum.

Sample distribution:

8 samples per year to be distributed in 2 batches with four serum samples of 350 µL each will be evaluated.

Reporting results:

Quantifications results of IgG, IgA, IgM, free kappa and lambda chains. Quantifications will not be evaluable, although the z-score and individual scores are included in the report just for information. In all cases the laboratory will report, presence / absence of paraprotein, and their typing. They will be collected separately up to 2 monoclonal serum components. If there were more, they should be entered in the comments' field, not being evaluable.

Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 4 weeks after receipt of samples.

Determination of the assigned value:

The altered components and their classification will be determined by consensus of will be determined by consensus of 75% of the participating laboratories. When this consensus were not reached, the item would be so named inconclusive and will not be evaluable. Quantification will be represented by the robust mean of results from participants and its corresponding uncertainty (ISO17043: 2010).

Scoring:

For a correct result to be considered coincident it must be coincident with the Assigned value.
For a concentration deemed correct, its z-score value must be within the acceptance range.

Scores:

- Qualitative results coincident with the assigned value: correct (0 points)
- Qualitative result does is not the same as assigned value: questionable result (1 point)
- z $\in$ (-2, 2) correct result (0 points)
- z $\in$ (-3, -2] U [2, 3) warning: questionable result (1 point)
- z $\in$ (-, -3] U [3,) action signal: incorrect result (2 points)

The accumulation of two or more points on a same parameter along two consecutive rounds evidences the occurrence of abnormalities 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 obtain two or less points in a same parameter and sending results of 7 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.

IQ-5 Urine paraproteins

Purpose:

Evaluate the performance of participants in the detection and typing of urine paraproteins.

Sample distribution:

8 samples per year to be distributed in 2 batches with four urine samples each with a volume of approximately 2 mL will be evaluated.

Reporting results:

Results of presence / absence of paraprotein will be collected. They will be noted down separately up to 2 monoclonal serum components. If there were more, they should be entered in the comments' field, not being evaluable.

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

Determination of the assigned value:

The altered components and their classification will be determined by consensus of will be determined by consensus of 75% of the participating laboratories. When this consensus were not reached, the item would be so named inconclusive and will not be evaluable.

Scoring:

For a correct result to be considered coincident it must be coincident with the Assigned value:

- Qualitative results coincident with the assigned value: correct (0 points)
- Qualitative result does is not the same as assigned value: questionable result (1 point)

The accumulation of two or more points on a same parameter along two consecutive rounds evidences the occurrence of abnormalities 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 obtain two or less points in a same parameter and sending results of 7 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.

IQ-6 Oligoclonal bands

Purpose:
Evaluating the performance of participants in the detection and characterization of oligoclonal bands in paired samples of serum - cerebrospinal fluid (CSF).

Sample distribution:

12 samples per year to be distributed in 2 rounds with 3 LCRs and their three paired sera of known IgG and albumin concentrations, with volumes of at least 0,15mL will be evaluated

Reporting results:

Quantifications of IgG in CSF and serum are provided by GECLID-SEI. In all cases the laboratory will report, presence / absence of oligoclonal bands in serum and CSF (intrathecal IgG synthesis) and its characterization (stripe pattern). Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 6 weeks after receipt of samples.

Determination of the assigned value:

The altered components and their classification will be determined by consensus of 75% of the participating laboratories. Not reached this consensus, it will be used to the consensus (laboratory with less than 2 points in the 2 previous rounds).When this consensus were not reached, the item would be so named inconclusive and will not be evaluable.

Scoring:

For a correct result to be considered coincident it must be coincident with the Assigned value.
Scores:

- Qualitative results coincident with the assigned value: correct (0 points)
- Qualitative result does is not the same as assigned value: questionable result (1 point)

The accumulation of two or more points on a same parameter along two consecutive rounds evidences the occurrence of abnormalities 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 obtain two or less points in a same parameter and sending results of 5 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.

IQ-8 Complement function

Purpose:

Evaluate the performance of participants in the functional evaluation of complement.

Sample distribution:

8 samples per year (serum + citrate plasma) to be distributed in 2 batches with four samples each (pairs plasma-serum), with an approximate volume of 0.25ml will be evaluated. The samples will be sent frozen, with dry ice.

Reporting results:

Within this scheme, results of haemolytic activity of the complement, CH50 and C1INH, will be recorded.

- Laboratories should include their own normal and negative controls to qualitatively assess the samples. The Steering Committee recommends that samples with results + / 5% of the cut-off should be reported as doubted.
- One of the samples sent will arbitrarily receive the functional value 100% and the rest will refer to it as a percentage, for the quantitative analysis of the results.
- Participants may determine (voluntary) C1inh concentration within samples, in order to make precise diagnoses, in the case of subtypes of HAE

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

Determination of the assigned value:

Quantification will be performed by the average robust results of the participants and their corresponding uncertainty. Qualitative results (normal function vs decreased function) will be assigned by consensus of the participants, it will be determined by consensus of 75% of the participating laboratories. When this consensus were not reached, the item would be so named inconclusive and will not be evaluable. Quantifications will be represented by the robust mean of results from participants and its corresponding uncertainty (ISO17043: 2010).

Scoring:

For a correct result to be considered coincident it must be coincident with the Assigned value.
For a concentration deemed correct, its z-score value must be within the acceptance range.

Scores:

- Qualitative results coincident with the assigned value: correct (0 points)
- Qualitative result does is not the same as assigned value: questionable result (1 point)
- $z \in (-2, 2)$ correct result (0 points)
- $z \in (-3, -2] \cup [2, 3)$ warning: questionable result (1 point)
- $z \in (-, -3] \cup [3,)$ action signal: incorrect result (2 points)

The accumulation of two or more points on a same parameter along two consecutive rounds evidences the occurrence of abnormalities 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 obtain two or less points in a same parameter and sending results of 6 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.

IQ-11: Response to Immunization

Purpose:

To evaluate the performance of participants in the evaluation of the response to vaccination against Pneumococcus and Salmonella sp

Sample distribution:

8 samples per year (4 pre immunization and 4post-vaccination) to be distributed in 2 batches with four serum samples of 350 µL each will be evaluated.

Reporting results:

Within this scheme results total IgG, anti-pneumococcus and anti-Salmonella spp. recorded.

Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 4 weeks after receipt of samples.

Determination of the assigned value:

Quantification will be performed by the average robust results of the participants and their corresponding uncertainty. Qualitative results (normal function vs decreased function) will be assigned by consensus of the participants, it will be determined by consensus of 75% of the participating laboratories. When this consensus were not reached, the item would be so named inconclusive and will not be evaluable. Quantifications will be represented by the robust mean of results from participants and its corresponding uncertainty (ISO17043: 2010).

Scoring:

For a correct result to be considered coincident it must be coincident with the Assigned value.
For a concentration deemed correct, its z-score value must be within the acceptance range.

Scores:

- Qualitative results coincident with the assigned value: correct (0 points)
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- z Є (-2, 2) correct result (0 points)
- z Є (-3, -2] U [2, 3) warning: questionable result (1 point)
- z Є (-, -3] U [3,) action signal: incorrect result (2 points)

The accumulation of two or more points on a same parameter along two consecutive rounds evidences the occurrence of abnormalities 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 obtain two or less points in a same parameter and sending results of 6 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.

IQ-14: Production of IFN-γ in response to pathogens

Purpose:

Evaluating the performance of participants in the assessment of by IGRAs (Interferon gamma release assays) as indicator of infection, the response to M. tuberculosis and other pathogens.

Sample distribution:

4 samples annually to be distributed in 2 deliveries with 2 samples (whole blood pairs of antigen and mitogen TB control) each will be evaluated

Reporting results:

Within this scheme results γIFN (IU / mL) n response to TB antigens will be recorded together with the test interpretation. Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 4 weeks after receipt of samples.

Determination of the assigned value:

Quantification will be represented by the robust mean of the participants' results and their corresponding uncertainty. Qualitative results will be assigned by consensus of the participants, it will be determined by consensus of 75% of the participating laboratories. When this consensus were not reached, the item would be so named inconclusive and will not be evaluable. Quantifications will be represented by the robust mean of results from participants and its corresponding uncertainty (ISO17043: 2010).

Scoring:

For a correct result to be considered coincident it must be coincident with the Assigned value.
For a concentration deemed correct, its z-score value must be within the acceptance range.

Scores:

- Qualitative results coincident with the assigned value: correct (0 points)
- Qualitative result does is not the same as assigned value: questionable result (1 point)
- z Є (-2, 2) correct result (0 points)
- z Є (-3, -2] U [2, 3) warning: questionable result (1 point)
- z Є (-, -3] U [3,) action signal: incorrect result (2 points)

The accumulation of two or more points on a same parameter along two consecutive rounds evidences the occurrence of abnormalities 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 obtain two or less points in a same parameter and sending results of 6 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.

IQ-15: Monitoring of anti TNFα therapies

Purpose:

Evaluating the performance of participants in the quantification of circulating antibodies against TNFα (human, chimeric fusion) and drug levels.

Sample distribution:

4 samples annually to be distributed in 2 deliveries with 2 serum samples of 350 µL each will be evaluated

Reporting results:

Within this scheme, results of antibodies directed against circulating anti TNF and biological drugs (anti-adalimumab, infliximab, and etanercept) together with drug levels will be recorded. Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 4 weeks after receipt of samples

Determination of the assigned value:

Quantification will be represented by the robust mean of the participants' results and their corresponding uncertainty. Qualitative results will be assigned by consensus of the participants, it will be determined by consensus of 75% of the participating laboratories. When this consensus were not reached, the item would be so named inconclusive and will not be evaluable. Quantifications will be represented by the robust mean of results from participants and its corresponding uncertainty (ISO17043: 2010).

Scoring:

For a correct result to be considered coincident it must be coincident with the Assigned value.
For a concentration deemed correct, its z-score value must be within the acceptance range.

Scores:

- Qualitative results coincident with the assigned value: correct (0 points)
- Qualitative result does is not the same as assigned value: questionable result (1 point)
- z Є (-2, 2) correct result (0 points)
- z Є (-3, -2] U [2, 3) warning: questionable result (1 point)
- z Є (-, -3] U [3,) action signal: incorrect result (2 points)

The accumulation of two or more points on a same parameter along two consecutive rounds evidences the occurrence of abnormalities 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 obtain two or less points in a same parameter and sending results of 6 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.

IQ-16: soluble CD25

Purpose:

Evaluating the performance of participants in the quantification of soluble CD25 in serum.

Sample distribution:

6 samples per year to be distributed in 2 deliveries with 3 serum samples of 100 µL each will be evaluated.

Reporting results:

Within this scheme soluble CD25 results will be recorded both in pg / mL and IU / mL. Obtained results can be sent exclusively by means of the web result's form. Data shall be recorded within 8 weeks after receipt of samples

Determination of the assigned value:

Quantification will be represented by the robust mean of the participants' results and their corresponding uncertainty.

Scoring:
For a concentration deemed correct, its z-score value must be within the acceptance range.

Scores:

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

The accumulation of two or more points on a same parameter along two consecutive rounds evidences the occurrence of abnormalities 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 obtain two or less points in a same parameter and sending results of 6 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.

CRITERIA / ELIGIBILITY

One set or result is allowed per laboratory within the subprogram.
For all schemes, laboratories participating in this sub-program should include their own positive and negative controls.
Schemes for all participants should note down the method used in the site provided for this purpose on the results' submission form.

SAMPLES specimens or items

Samples

Samples within 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 (serum, plasma), although for concrete schemes are distributed urine and cerebrospinal fluid. They are distributed in aliquots of different volumes depending on the scheme. All handling of CSF samples will be conducted under sterile conditions. Samples will be maintained and sent at room temperature within a period of 36h from extraction.
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-SEI 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.

SAMPLES BY DESIGN: for certain schemes can prepare samples with specific manipulations that emulate sera from different pathologies.

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-SEI 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-SEI 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 abnormalities that should be investigated and corrected by the laboratory (2). The criteria for Scores will be reviewed annually by GECLID-SEI on the basis of the quality standards for providers of interlaboratory comparison (2) 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.
- Results of individual participation in the Interlaboratory comparison and obtained scores
- LEM report (laboratories, equipment and methods) collecting the frequencies of participation, methods and reagents used

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-SEI 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.splink.es. This certificate shall be issued by GECLID-SEI 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.

COMPLAIN's POLICY

To formalize a claim, you must fill in the document <Model Claim> available on the website of all the schemes and make them reach those responsible for the program by email, using the <Claims: Submission Tool>, web tool found in all schemes. Your complaints will be first reviewed by 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 complaint progress. Remember that the deadline for complaints ends up 1 month after reports are published. **Remember that the deadline for claims to each round of shipments will always be closed 1 month after the publishing of reports.**

If the claim is related to transcription errors of results, you should always provide the original records of the analysis. Such claims from May 2019 are sent to the appropriate Steering committees.

REFERENCES

1.ISO-IEC 17043: 2010 Conformity Requirements for Proficiency Testing assessment. General. International Organization for Standardization, 2010
2. ISO 13528: 2015 Statistical methods for use in proficiency testing by interlaboratory comparisons