QUALITY SYSTEM INFORMATION

QUALITY SYSTEM **qs@biogroupmedicalsystem.com**

Date	Rev.	Reason	Drafting of document	Approval	Archiviazione
29/03/2019	00	First Issue	COP	RQS	RGQ
06/11/2019	01	Variation Point 6.1 Exclusion from processing			
31/03/2020	02	Introduction of Hematology test			
07/04/2020	03	Modification in point 2,3 and 5			

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CLINICAL CHEMISTRY AND IMMUNOLOGY LEVEL 1 PROFICIENCY TESTING

General information on the organisation and management

Organizer **Registered office and headquarters**	Bio-Group Medical System S.r.l. – Divisione Quality System Loc. Campiano 9/B 47867 Talamello (RN)-Italy PHONE:+39 0541 920686 FAX: +39 0541 922130 MAIL: qs@biogroupmedicalsystem.com
Subcontracted activities	• Preparation of the proficiency test items The QS Division uses highly qualified, certified suppliers in compliance with the provisions specified in the standard 17043:2010 • Homogeneity and stability tests The data issued by accredited supplier/according to UNI EN ISO/IEC 17025:2018 and UNI EN ISO/IEC 15189:2013 is checked by the coordinator who evaluates its compliance. Homogeneity and stability data are available for consultation at the company for a minimum period of four years.
Main reference document	UNI CEI EN ISO/IEC 17043:2010 Conformity assessment – General requirements for collaborative proficiency testing UNI EN ISO 9000:2005 Quality management systems - Basic principles and terminology ISO 13528:2015 Statistical methods for use in proficiency testing by interlaboratorycomparisons JCGM 100 :2008 Evaluation of measurement data – Guide to the expression of measurement uncertainty UNI ISO 5725 – 1-6:2004 Accuracy (trueness and precision) of results and measurement methods, Part 1, 2, 3, 4, 5, 6. ILAC G13:08/2007 Guidelines for the Requirements for the Competence of Providers ofProficiencyTestingSchemes UNI CEI 70099:2008 International Metrology Glossary -Basic and general concepts and related terms (VIM)

1. Introduction

The clinical analysis laboratory has as its ultimate goal the generation of data about the health of the patient, data that will be used later in the diagnostic process. For this purpose, it plays a leading role in defining the behaviour that a clinician should follow to deal with a diagnosis or a follow-up treatment or a condition.

Therefore, the work carried out in a clinical analysis laboratory must follow a series of quality procedures in order to obtain a final data that meets the required precision and accuracy criteria.

Each laboratory must be able to work in compliance with the quality rules to ensure that the generated reports are as accurate as possible. The data output by clinical analysis is subjected to systematic and random errors. If the operator knows the magnitude of these errors, this will compensate system errors and provide experimental data as close as possible to reality.

The repeatability of the same analysis under the same working conditions (verified by means of internal checks) is a first approach in assessing the errors. The comparison with a multiparty agreed mean value ensures and validates the data assessed by internal checks.

The Quality System represents an external Quality Assurance (EQA), i.e. it consolidates or provides guidance for strengthening the approach to quality control of the laboratory.

2. Condition for participation and registration for PT

The QS is open to: clinical analysis laboratories, multispecialist diagnostic centres, nursing homes and similar entities**.**

Expected number of participants; Given the many years of experience of QS Division in this field, we expect a number of 150 participants.

The registration can be done directly by the laboratory concerned or by Distributors. In the case of direct entitlement by the laboratory or from Distributors throughout Italy, the person in charge at the centre sending the request must complete the registration form in all its parts, and send it (MOD.18), as well as the contract and the customer Privacy Policy.

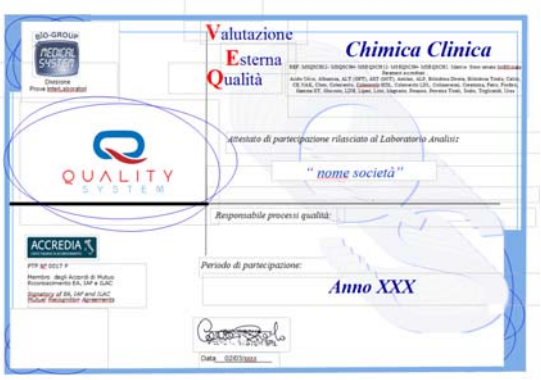
In the case of registration via a foreign Distributor, the latter must compile the form 27, specifying the data of the testing labs and the selection of the relative proficiency testing.

The participant must ensure the following:

- Internet access
- PDF Reader
- Internet Browser (Firefox - Chrome)

After verifying the conditions listed above, the QS division will proceed with the registration of the centre by sending the website access credentials (User and Password) and detailed instructions for participation in the proficiency test and the QS Calendar by email or by enclosing the relative documents in a parcel upon the first delivery.

The **participation certificate** for the current year will be issued the first time the OPV is submitted.



The packaging of OPV sent contains the method of use form IFU.
This document INFO is also available on the website of the Bio-Group MEDICAL SYSTEM Quality System Division.
In case of changes to the programming or if a Supplement to the reviewed Test Report is issued, participants are timely informed via e-mail.

Upon each delivery, the system participants will receive:

- *The test samples*
- *Instruction for use (IFU)*
- *A letter of introduction* describing the material sent and how to use it.

The participant can contact at any time the Quality Control Division of Bio-Group Medical System, which is available for any clarifications or issues concerning the processed data, either by calling 0541920686, room 3 or sending an email to qs@biogroupmedicalsystem.com

3. Test Materials

The proficiency testing items are Human Lyophile Serums or Control blood simulating the biological findings usually measured by the participants. These Control samples will present a range of values completely comparable with those found in the working routine of the participants. To this end, the coordinator will choose Control samples which give measurements that can be referred to both physiological and pathological intervals.
The operating instructions are shown in a document identified by the acronym ISTRU.
The test methods are freely chosen by each participating laboratory.
In compliance with the provisions of UNI CEI EN ISO/IEC 17043:2010 (p.to 4.6.1.2), test samples must be treated in the same manner as that applied for the samples tested in the routine procedure.
For each test parameter is required a single determination.

Test list:

- Clinical Chemistry 12 monthly samples level 1 MSQSCH12-MSEQSCH12
- Clinical Chemistry 4 quarterly samples level 1 MSQSCH4 - MSEQSCH4
- Clinical Chemistry 1 sample, level 1 MSEQSCH1
- Immunology 12 monthly samples level 1 MSQSI12-MSEQSI12
- Immunology 4 quarterly samples level 1 MSQSI4 - MSEQSI4
- Immunology 1 sample, level 1 MSEQSI1
- Hematology 8 parameters monthly 12 samples MSQSE812-MSEQUALITYE12
- Hematology 8 parameters quarterly 4 samples MSQUALITYE8-MSEQUALITYE8
- Hematology 8 parameters 1 sample Year MSEQSE8

The tested parameters are as follows:

Clinical Chemistry level 1: Bile Acids*, Uric Acid, Albumin, ALT (GPT), AST (GOT), Amylase, ALP, Bicarbonates*, Direct Bilirubin, Total Bilirubin, Calcium, CK NAK, Chlorine, Cholesterol, HDL Cholesterol, LDL Cholesterol, Cholinesterase, Creatinine, Iron, Phosphorus, GT Range, Glucose, LDH, Lipase, Lithium, Magnesium, Potassium, Total Protein, Copper*, Sodium, Triglycerides, UIBC*, Urea, Zinc*.
Test Coordinator: Dr. Montini Matteo – QS Division of Biogroup Medical System S.r.l.
* Parameters not covered by ACCREDIA accreditation

Immunology level 1: 25 OH Vitamin D, ACTH*, Alpha-Fetoprotein, C Peptide*, CA 125, CA 15-3, CA 19-9, Carbamazepine*, CEA, Cortisol, DHEA Sulphate*, Digoxin*, Estradiol, Ferritin, Folates, FSH, FT3, FT4, β-HCG, HGH*, IgE, Insulin*, PTH*, LH, Phenobarbital*, Phenytoin*, Progesterone, Prolactin, PSA-FREE, PSA, T3, T4, Testosterone, TGAB*, Theophylline*, Thyroglobulin*, TMAB*, TPO AB*, TSH, Valproic Acid*, Vitamin B12*

Hematology: Erytrocites (RBC), Leucoiyes (WBC), Hemoglobin (HB), Hematocrite (HCT), Mean cells volume (MCV)*,Mean cell haemoglobin concentration (MCHC), Red Distribution Width (RDW), Mean haemoglobin contain (MCH), Platellets (PLT), Mean platellets volume (MPV).
Test Cordinator Dr. Matteo Montini- Divisione QS di Biogroup Medical System Srl

*Parameters not covered by ACCREDIA accreditation
The proficiency test involves 1/4/12 determinations per year depending on the selected frequency.
Each test material is tested by the QS Division based on the COP, ensuring the requirements of uniformity and stability according to the goals required for the test. The tests will be carried out on a number of statistically significant rates according to the instructions contained in the reference standard ISO 13528:2015.
In the case of a failure of these testings, the material shall not be distributed and the test will be scheduled again, giving timely notice about the test to the members.
The test material is preserved until the publication of the last test report of the relative PT.

4. Test aim

The purpose of the QS is to allow a comparison between independent laboratories. The external quality evaluation statistically examines the end result of all the work process taking into account: the pre-analytical phase, the analytical phase, and finally the post analytical phase that involves reporting and last transmission of the data.
The control results allow making deductions on the good functioning of both the process itself as an organised structure and the various phases of which it is composed; in some cases, they also allow obtaining suggestions on the type of problem that prevents it from obtaining a good result.

In other words, the participation in QS programs is a valuable tool for assessing the diagnostic quality of a laboratory.
The periodic control obtained via QS allows the operator to assess his analytical system by comparing the results obtained with those of the daily IQC, thus validating the latter and the entire organisation.
QS offers precise indications on any possible anomaly and is, therefore, a powerful tool for the constant improvement of the "Total Quality" and data quality assurance.

5. Test execution timelines

5.1 Distribution date and frequency for immunology and clinical chemistry PT

"Quality System" provides for the sending of samples to be analyzed according to the valid calendar mod. CAL (also available on the QS website). Subscriptions are accepted at any time of year, samples will be sent from the current period to the end of the year. In the event that the shipping dates cannot be respected, the participants will be informed by e-mail. The determinations and the sending of the results via the web interface, must be carried out as per the calendar mod. CAL.

5.1.1 Dates and frequency of distribution of Hematology tests

In order to ensure the performance of the tests within the declared stability of the control blood sent as an OPV for the hematology tests and to guarantee an acceptable interval between issue of the test report and execution of the subsequent test to allow the participant to implement of corrective actions in a reasonable time, the hematology test follows the following deadline calendar.

5.2 Method of distribution

Samples are sent by courier within the date set in the shipping calendar mod. CAL. The material is shipped to the headquarters of each laboratory directly registered or to distributors who guarantee the shipment to the laboratories within the time limits and conditions as per the related agreement. Any problems in receiving the material (delays beyond the expected 7 days, anomalies in the packaging or appearance, spilling of the material from the bottle, etc.) must be promptly reported to the QS Laboratory Testing Division. The availability of public offerings in addition to those distributed is guaranteed, limited to cases of non-delivery by the carrier in charge or accidental damage, in any case not beyond the time limits set for the execution of the determinations.

5.3 Transmission of results

The results are transmitted within the deadline established by QS CALENDAR (mod. CAL), via the secured area of the website qs-veq.it , by selecting the test in question; to access please enter the User and the Password referred to herein on p. to 7.

To facilitate data entry, upon the first access to the website's home page, you will have to set up the Data entry tables where the participant will insert the tools and the methods used for the tests. Depending on the provisions under section 5.5.3 of ISO 13528:2015 standard, the results must always be expressed in numerical form. Results of the type “<…”, “ below or above the detection limit” are not allowed.

Each program has a different electronic report sheet containing specific mandatory fields that must be compiled in order to proceed to the processing phase.

For each parameter will be required:

1) METHOD: the main analytical methods used by the laboratories are available for selection
2) UNIT OF MEASUREMENT
3) INSTRUMENT
4) VALUE obtained after the examination of the samples.

All four data MUST be reported under penalty of exclusion from the statistical processing, as it is difficult to include them in a class of approval.

5.4 Issuance of the Test Reports

The test reports will be published in the reserved area of the website on the date established in the valid calendar (mod. CAL), except for exceptions previously communicated.

Participants who do not send the results within the deadline will not have an accredited test report.
Test reports will be available for four years from the date of publication.

6. Evaluating the performance of laboratory and statistical treatment of data

In order to provide an instrument that allows the participant to make an immediate and unambiguous assessment of the quality of the examination, the QS Division shall carry out the statistical analysis in accordance with ISO 13528:2015, as follows:

- The value assigned to each measurement is represented by the consensus mean calculated according to algorithm "A" ISO 13528:2015, which allows the exclusion of aberrant values from the mean, making this consensus mean scarcely influenced by incorrect values

- The measurement uncertainty of the assigned value is calculated based on standard deviation by the formula: $U(X_{pt}) = 1{,}25\left(\frac{s}{\sqrt{p}}\right)$ where:

  - s: robust standard deviation

o p: number of participants

- Rejected type σ: calculated using the formula σ_{pt}= RSD% * x_{pt} where RDS% is the relative standard deviation calculated on the historic value of the parameter and x_{pt} is the approval mean of the parameter
- Laboratory performance evaluation is expressed by Z-index calculated as follows: $Z = \frac{(x-X)}{\sigma}$ where x is the average of approval, X is the value of the participant and σ is the standard deviation, and the Z-index is calculated as follows:

$$Z' = \frac{(x_i - x_{pt})}{\sqrt{\sigma_{pt}^2 + u^2(x_{pt})}}$$

Where $u^2(x_{pt})$represents the uncertainty of measurement

- Since it concerns an assessment of the performance of the approval mean , the Z-score and Z'-score indices are used interchangeably:
  Z-score: this is calculated when the measurement uncertainty is negligible or$u(x_{pt})$< 0.3 σ_{pt}.
  Z'-score: this is calculated when the measurement uncertainty is not negligible or $u(x_{pt})$>0.3 σ_{pt}.

Typically the absolute Z value obtained by the participant provides the indications summarised in the following table:

|□|≤2 indicates "satisfactory" performances and does not generate any signal

2.0<|□|<3.0 indicates "questionable" performances and generates a Warning signal

|□|≥3.0 indicates "unsatisfactory" performances and generates an Action signal

Each measurement is also provided with a Shewart chart that allows assessing, for the purpose of self-improvement, the performance monitoring over time.

6.1 The following were excluded from processing

The measurements entered and affected by coarse error (i.e.: typographical error 2.1 instead of 21) will be excluded from processing; the participant will receive from the test Coordinator by email the measurement excluded and detailed reason for exclusion.

For statistical populations of less than 20 participants but above 15, the outlier measures are excluded by using the Grubbs Test. The participant will receive notification of the exclusion.

Statistical populations with less than 15 participants but more than 5 will be processed outside accreditation and will receive an indicative performance index.

All subsets statistics whose number of participants is less than 5 are excluded from processing. Also in this case, the test Coordinator will notify participants by email.

6.2 Issuance of the test reports

The Coordinator can communicate the cancellation of a test report in the event of serious incidents.

He shall reissue the test report indicating the review status.

7. Confidentiality

QS in the test report will use the registration code assigned to the same test as the only identifying element of the data source. The code is known only to the QS and the laboratory Division. If the OPVs are shipped to the distributor, the code is also known by the latter.

The participant must ensure that both the USER and the password assigned during registration will not be disclosed to third parties; at the same time, QS Division assumes the obligation of confidentiality in this respect.
The participant may agree to waive anonymity in order to:

- discuss his/her own results;
- establish a process of mutual assistance to improve their skills and performance;
- use the results for the purposes of external recognition (accreditation, etc.);
- communicate results to the competent authorities, which in turn may request that the same results are delivered in an official form by COP.

The test report that is available only on the reserved area of the website qs.biogroupmedicalsystem.com, is accessible to every participant and the Quality System division.
The participant agrees not to share information with others about the results of the determinations made in the course of the Test.
In the presence of objective evidence of collusion between attendees or falsifying results, QS reserves the right to exclude from the test any subjects who have been guilty of such conduct.

8. Complaints and appeals

Participants in the tests who intend to submit Appeals/Complaints relating to aspects

connected to the execution of the Tests, must submit a written request, enclosing the necessary

documentation. Such request shall be sent to the mail address qs@biogroupmedicalsystem.com, addressed to the Coordinator of the test.