QUALITY SYSTEM

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29/03/2019	00	First issue	COP	RQS	RGQ
06/11/2019	01	Change point 6.1 Exclusion from processing			
31/03/2020	02	PT Hematology Insertion			
07/07/2020	03	Points variation 2-3-5			
26/05/2022	04	Company Change			
02/05/2023	05	Changes following observations no. 2 and 11 of the ACCREDIA inspection visit of 04/08/2022			
25/03/2024	**06**	**Change following observation no. 6 of the ACCREDIA inspection visit of 31/01/2024**			

EVALUATION TESTS CLINICAL CHEMISTRY, IMMUNOLOGY and HEMATOLOGY monthly/quarterly

General information on organization and management

Organizer Registered office and operational headquarters	Bio-Group Medical System Srl – Quality System Division Registered office: Via Latina, 20 – 00179 Rome Headquarters: Loc. Campiano 9/B - 47867 Talamello (RN)-Italy PHONE: +39 0541 920686 FAX: +39 0541 922130 E-MAIL: qs@biogroupmedicalsystem.com
Subcontracted activities	• Preparation of the evaluation test objects QS Division uses highly qualified suppliers, certified and compliant with the standards set by the 17043:2010 regulation • Homogeneity and stability tests The data released by the accredited/compliant supplier to the UNI EN ISO/IEC 17025:2018 and UNI EN ISO/IEC 15189:2013 standards are viewed by the coordinator who evaluates their conformity. The homogeneity and stability data are available for consultation at the organization for a minimum period of four years.
Main reference document	UNI CEI EN ISO/IEC 17043:2010 Conformity assessment – General requirements for interlaboratory proficiency testing UNI EN ISO 9000:2015 Quality management systems – Fundamentals and vocabulary. ISO 13528:2015 Statistical methods for use in proficiency testing by interlaboratory comparisons JCGM 100 :2008 Evaluation of measurement data – Guide to the expression of uncertainty in measurement UNI ISO 5725 – 1-6:2004 Accuracy (trueness and precision) of measurement results and methods, Part 1, 2, 3, 4, 5, 6. ILAC G13:08/2007 Guidelines for the Requirements for the Competence of Providers of Proficiency Testing Schemes

	UNI CEI 70099:2008 International Vocabulary of Metrology - Fundamental and general concepts and related terms (VIM)

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1. Introduction

The clinical analysis laboratory has as its final goal the generation of data on the patient's health status that will subsequently flow into the diagnostic process. For this reason, it plays a primary role in defining the behavior that a clinician must follow to face a diagnosis or a follow-up of a therapy or a condition.

The work that is carried out in a clinical analysis laboratory, therefore, must necessarily follow a series of procedures within a concept of quality to obtain a final data that respects the characteristics of precision and accuracy.

Every laboratory must be able to work in the best possible way respecting quality rules so that the reports produced are as close as possible to reality. The data that comes from a clinical analysis can be affected by systematic and/or random errors. The more the operator knows the extent of these errors, the more he will be able to compensate the system by providing experimental data that is as close as possible to the real one.

The repeatability of the same analysis under the same working conditions (verified by using internal controls) is a first approach for the evaluation of errors. The comparison with a consensus average of several participants ensures and validates what was evaluated with internal controls.

Quality System represents an external Quality Assurance (EQA), that is, it provides indications to consolidate the laboratory's approach to quality control.

Quality System is the trademark of the VEQ of Bio Group Medical System, Italian Proficiency Testing Provider.
The Proficiency Testing Providers are responsible for the organization of the interlaboratory evaluation tests (VEQ), from the design to the choice and preparation of the objects, to the checks of homogeneity and stability of the materials, to the distribution of the samples to the participants, to the statistical analysis of the data up to the evaluation of the results and the issuing of the report with the performances of the participants.

The activity carried out by Proficiency Testing Providers, therefore, is fundamental to allow participating laboratories to monitor their performance over time, through continuous participation.

Accreditation as an organizer of interlaboratory proficiency tests in compliance with the UNI CEI EN ISO/IEC 17043:2010 standard demonstrates the technical competence of the organizer to design, organize and manage the tests indicated in the accreditation field. The organizer of interlaboratory proficiency tests is in fact responsible for ensuring that the technical and management requirements,

specified in the reference standard, are also satisfied by the collaborators and subcontractors involved in the test schemes subject to accreditation.

~~**As far as the Accredia mark is concerned, it constitutes the formal demonstration of the competence, independence and impartiality of the organizer of the evaluation test by the National Accreditation Body. This mark also constitutes a tool and an opportunity to foster the trust of participants in the service provided as a guarantee of its quality .**~~

Bio Group Medical System is a PT Provider accredited ISO 17043:2010 by ACCREDIA (certificate no. 17/P and related attachment downloadable from the website https://www.accredia.it/ banche-dati/).

Participating in UNI EN ISO 17043 accredited EQA programs offers numerous advantages for the laboratory, including:

- **Technical competence verification**
  Accreditation guarantees the technical competence of QUALITY SYSTEM for external quality assessment. This allows the participating laboratory to compare its performance with that of other laboratories on an impartial and objective basis; evaluating:
  . competence in measurement and analysis activities.
  . any weaknesses in testing methods, promoting continuous improvement

- **Regulatory compliance**
  Participation in QUALITY SYSTEM allows you to:
  . Meet the requirements of national and international regulations and standards.

- **Strengthen your position in inspections and audits by demonstrating that your laboratory actively participates in quality assurance programs.**

Continuous improvement

The feedback obtained from the VEQ results allows to:

- **Correct any errors or deviations in the measurement processes.**
- **Improve the quality of services offered to patients, reducing the risk of non-compliance**
- **Updating staff skills through benchmarking data analysis.**

The UNI EN ISO 17043 accreditation ensures:

- **Impartiality and transparency: Interlaboratory tests are managed without external influences and the results are provided in a clear and understandable way, ensuring the independence of the process.**
- **Technical competence: QUALITY SYSTEM is subject to regular audits by the accreditation body, which certifies the competence in managing VEQ programs.**
- **Quality Control: Internal processes are continuously monitored and improved to accurately assess any potential errors affecting participant measurements.**

2. Conditions for participation and registration in the PT

The following can join the QS: clinical analysis laboratories, multi-specialist diagnostic centres, nursing homes and similar institutions **.**

Expected number of participants: Given the many years of experience of QS Division in the sector, it is assumed that we can count on a number of 150 participants.

Registration is carried out directly by the interested laboratory or through Distributors. In the case of direct membership by the laboratory or by Distributors Italy , the person in charge of the center that sends the request must have filled in all its parts and sent the registration form (MOD.18), the contract and the customer information Privacy.

In the case of membership through a foreign distributor, the latter will fill out form 27, summarizing the data of the analysis laboratories and the selection of the relative evaluation tests.

The participant must ensure the availability of:

- Internet access
- PDF Reader Program
- Internet browsing browser

After having verified the above conditions, the QS division will proceed with the registration of the center by sending the website access credentials (User and Password), the detailed instructions (ISTRU) for participation in the evaluation test and the calendar (mod. CAL) by email or in paper format.

With the first submission of OPVs, the **certificate of participation** for the current year is issued.

The OPV package shipped contains the operating and use instructions mod. IFU.
This INFO document can also be consulted on the website of Bio-Group MEDICAL SYSTEM, Quality System division.
In case of changes in the schedule or in case of the issuance of revised Test Reports, participants will be promptly informed by e-mail.

With each submission, system members receive:

- *Samples to be analyzed*
- *IFU Operating and Use Instructions*
- *Cover letter*

The participant may always contact the Quality Control Division of Bio-Group Medical System which is available for any clarifications or problems relating to the processed data by calling 0541920686 ext.3 or by sending an e-mail to qs@biogroupmedicalsystem.com

3. Test materials

The objects of the evaluation tests are materials simulating the biological sample usually analyzed by the participant for the test object of the test. These samples will present a range of values completely comparable

with those found in the participants' work routine. To this end, the coordinator chooses those samples that will give measurements referable to both physiological and pathological intervals.
The operating instructions and the relevant storage method are reported in the IFU operating instruction.
The test methods are freely chosen by each participating laboratory.
In compliance with the recommendations of the UNI CEI EN ISO/IEC 17043:2010 standard (point 4.6.1.2), the test samples must be treated in the same way as the samples analysed on a daily basis. For each test parameter, only one determination is normally required.

List of tests:

- Clinical Chemistry 1 monthly level 12 samples MSQSCH12-MSEQSCH12
- Clinical Chemistry 1 level quarterly 4 samples MSQSCH4 - MSEQSCH4
- Clinical Chemistry 1 level 1 sample MS EQSCH1
- Immunology 1 monthly level 12 samples MSQSI12-MSEQSI12
- Immunology 1 level quarterly 4 samples MSQSI4 - MSEQSI4
- Immunology 1 level 1 sample MSEQSI1
- Hematology 8 parameters monthly 12 samples MSQSE812-MSEQUALITYE12
- Hematology 8 parameters quarterly 4 samples MSQUALITYE8-MSEQUALITYE8
- Hematology 8 parameters Annual 1 sample MSEQSE8

The parameters to be tested are the following:

Clinical Chemistry 1st level : 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, Gamma GT, Glucose, LDH, Lipase, Lithium, Magnesium, Potassium, Total Proteins, Copper*, Sodium, Triglycerides, UIBC*, Urea, Zinc*.
Test Coordinator: Dr. Montini Matteo – QS Division of Biogroup Medical System Srl
* Parameters not covered by ACCREDIA accreditation

Immunology 1 level : 25 OH Vitamin D, ACTH*, Alpha-Fetoprotein, C Peptide*, CA 125, CA 15-3, CA 19-9, Carbamazepine*, CEA, Cortisol, DHEA Sulfate*, 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*
Test Coordinator: Dr. Montini Matteo – QS Division of Biogroup Medical System Srl

Hematology 8 Parameters: Red blood cells (RBC), White blood cells (WBC), Hemoglobin (HB), Hematocrit (HCT), Mean corpuscular volume (MCV)*, Mean corpuscular hemoglobin concentration (MCHC), Red blood

cell distribution width (RDW), Mean corpuscular hemoglobin content (MCH), Platelets (PLT), Mean platelet volume (MPV).
Test Coordinator: Dr. Montini Matteo – QS Division of Biogroup Medical System Srl

*Parameters not covered by ACCREDIA accreditation

The evaluation test includes, depending on the chosen frequency, 1 / 4 / 12 determinations per year.
Each test material is subjected to checks by the QS Division in the COP function, ensuring the homogeneity and stability requirements according to the objectives required for the test itself. The tests are performed on a statistically significant number of aliquots according to the indications contained in the reference standard ISO 13528:2015.
In the event of a negative outcome of these checks, COP will inform RQS, which will decide whether to cancel the test and promptly inform those enrolled in the test.
The test material is retained until the publication of the last test report of the relevant PT.

4. Purpose of the tests

The purpose of QS is to allow a comparison between independent laboratories. The external quality assessment statistically examines the final result of the entire work process, therefore taking into account: the pre-analytical phase, the analytical phase and, finally, the post-analytical phase which concerns the reporting and final transmission of the data.
From the results obtained with this control, deductions can be made on the good functioning of both the process itself as an organised structure, and of the various phases of which it is composed, arriving, in some cases, at obtaining suggestions on the type of problem that leads away from a good result.

Participation in QS programs, in other words, constitutes a valid tool for quality assurance of a laboratory.
The periodic control obtained through QS allows the operator to evaluate his analytical system by comparing the results obtained with those of the daily CQI, thus validating it and the entire organization.
QS provides precise indications on any anomaly and therefore turns out to be a powerful tool for the constant improvement of “Total Quality” and data quality assurance.

5. Test execution timing

5.1 Dates and frequency of distribution

“Quality System” provides for the sending of samples to be analyzed according to the current calendar mod. CAL (available on the QS website) . Subscriptions are accepted at any time of the year, OPVs will be sent from

the current period to the end of the year. In the event that the shipping dates cannot be respected, participants will be informed by e-mail.
The determinations and sending of results via the web interface must be carried out as per the CAL form calendar.

5.2 Distribution methods

OPVs are shipped by courier by the date set in the shipping calendar mod. CAL. The material is shipped to the headquarters of each registered laboratory directly or to distributors who guarantee shipment to the laboratories within the time limits and conditions as per the contract. Any inconvenience in receiving the material (delays beyond the expected 7 days, anomalies in the packaging or appearance, material leaking from the bottle, etc.) must be promptly reported to the QS Laboratory Testing Division. The availability of OPVs 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 carrying out the determinations.

5.3Transmission of results

The results are transmitted, within the deadline established in the current calendar (CAL form), through the reserved area of the qs-veq.it website, by selecting the test in question; User and Password are always used for access.
To facilitate data entry operations, upon first access to the home page of the site, the configuration of the Data entry tables is required where the participant will insert tools and methods used for the tests. According to what is reported in paragraph 5.5.3 of the ISO 13528:2015 standard, the results must always be expressed in numerical form. Therefore, results of the type “<…”, “lower than the detection limit” etc. are not permitted.
For each program there are different electronic reporting forms, for each of which the mandatory compilation of specific fields is required, in the absence of which it is impossible to proceed with the processing.

For each parameter you will be asked:

1) METHOD: the main analytical methods used by laboratories are present
2) UNIT OF MEASURE
3) INSTRUMENT
4) VALUE obtained from the examination of the samples.

All four of these data MUST be reported, otherwise they will be excluded from the statistical processing, making it difficult to insert them into a consensus class.

5.4 Issuing Test Reports

The test reports will be published in the reserved area of the website on the date established in the currently valid calendar (CAL form), unless previously communicated.

Participants who fail to submit their results by the deadline will not be eligible for an accredited test report. Test reports will be available for four years from the date of publication.

6 Evaluation of laboratory performance and statistical treatment of data

In order to provide a tool that allows the participant an immediate and unambiguous evaluation of the quality of the exam, the QS division in accordance with the ISO 13528:2015 standard performs the statistical analysis as follows:

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

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

- Standard deviation σ: calculated according to the formula σ_{pt}= RSD% * x_{pt}d where RDS% is the relative standard deviation calculated on the parameter's history and $x_{pt}$is the consensus mean of the parameter
- The evaluation of the laboratory performance is expressed by the Z index calculated as follows: $Z = \frac{(x-X)}{\sigma}$where x is the consensus mean, X is the participant's measurement and σ is the standard deviation, and by the Z' index calculated as follows:
$$Z' = \frac{(x_i - x_{pt})}{\sqrt{\sigma_{pt}^2 + u^2(x_{pt})}}$$
Where $u^2(x_{pt})$represents the measurement uncertainty

- Since this is a performance evaluation on a consensus average, the Z-score and Z'-score indices are used alternatively:

Z-score: is calculated when the measurement uncertainty is negligible i.e. $u(x_{pt})$< 0.3 σ_{pt}.
Z'-score: is calculated when the measurement uncertainty is non-negligible $u(x_{pt})$>0.3 σ_{pt}.

Typically the absolute value of Z obtained by the participant from indications summarized in the following scheme:

$|Z|$ ≤2 indicates "satisfactory" performance and does not generate any signal

2.0<$|Z|$<3.0 indicates "questionable" performance and generates a warning signal

$|Z|$ ≥3.0 indicates "unsatisfactory" performance and generates an intervention or Action signal

For each measurand, the Shewart graphic representation is also provided, which allows for the evaluation of performance monitoring over time for self-improvement purposes.

6.1 Exclusion from processing and late results.

The entered measurements affected by a gross error (e.g. typing error 2.1 instead of 21) will be excluded from processing;

For statistical populations with fewer than 20 participants but more than 15, outlier measures are excluded using the Grubbs Test. The participant will be notified of the exclusion.

All statistical subpopulations whose number of participants is less than 5 are excluded from the processing. In this case the Coordinator of the test will inform the interested participants by email.

If the measurements are entered after the last date for entry, the Z-score, D and D% fields will show "NA" (not applicable). Also on the last page (summary) in these cases "NA" is shown on the last 4 columns of the table (Z/Z' , Z-score, D%, Remark). Also late results will not be displayed in the shewart plot.

6.2 Reissue of test reports

The Coordinator may communicate the cancellation of a test report in case of serious anomalies.
It will reissue the test report indicating its revision status.

7. Confidentiality

In the test report QS will use the code assigned during registration for the test itself as the only identifying element of the data source. The code is known only to the QS division and the laboratory in question. In the case where the OPVs are sent to the distributor, the code is also known to the latter.

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

- discuss your findings;
- establish a process of mutual assistance to improve one's skills and performance;
- use the results for external recognition purposes (accreditation, etc.);
- communicate the results to competent authorities, who in turn may request that the same results are provided officially by COP.

The test report, as it can only be downloaded from the reserved area of the dedicated website, is accessible to each individual participant and to the Quality System division. The test reports are available for 4 years from their issue.
The participant undertakes not to exchange information with others regarding the results of the determinations carried out during the Test.
In the presence of objective evidence of collusion between participants or falsification of results, QS reserves the right to exclude from the test any subjects found to be responsible for such behavior.

8.Reports, Complaints and Appeals

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

connected with the carrying out of the Tests, must submit a written request, accompanied by the necessary documentation.

This request must be submitted to the email address qs@biogroupmedicalsystem.com and addressed to the test coordinator.