IFCC EXTERNAL QUALITY ASSESSMENT SCHEME FOR (CANDIDATE) CALIBRATION LABORATORIES IN LABORATORY MEDICINE

PROCEDURES

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1. Contents

2. Preamble

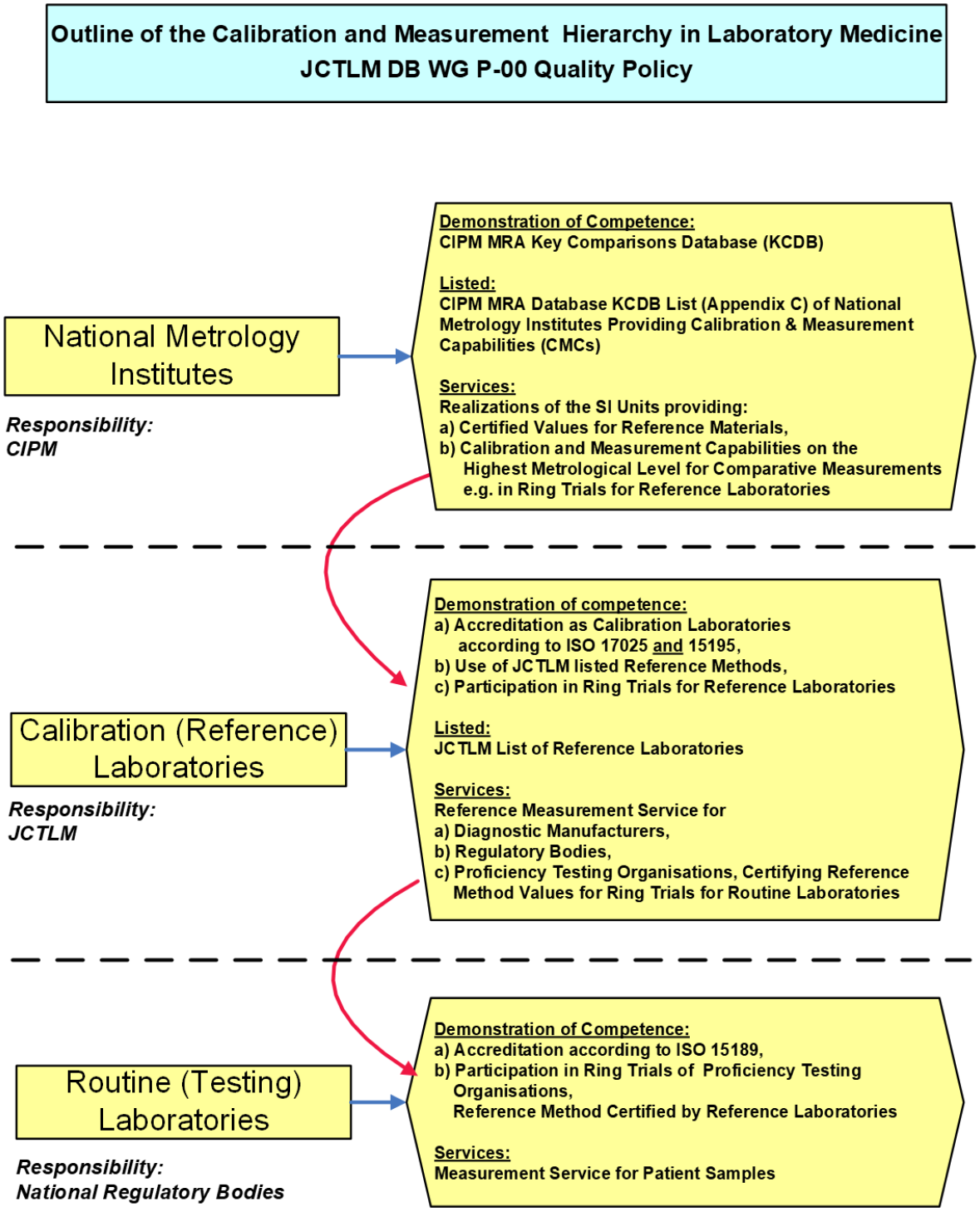
The concept of metrological traceability provides the most important strategy to establish standardization in laboratory medicine aiming at accurate measurement results independent of the principle of measurement, the actual measurement procedure (e. g. the commercial test kit) as well as the laboratory where such clinical testing is performed. The implementation of the concept of metrological traceability requires the availability of

- reference materials,
- reference measurement procedures (RMP), and
- reference services.

Therefore, the Joint Committee on Traceability in Laboratory Medicine (JCTLM) has been established by four organizations: The International Federation of Clinical Chemistry, Laboratory Medicine (IFCC), the International Bureau of Weights and Measures (BIPM), the International Laboratory Accreditation Co-operation (ILAC), and the International Council for Standardization in Haematology (ICSH). The objective of the JCTLM is to identify and publish lists of reference materials, reference procedures and reference services.

There exists a hierarchy of laboratories which is demonstrated in FLOW CHART 1and described in more detail in the JCTLM Database Working Group Quality Policy (JCTLM DB WG P-00) of JCTLM DB WG.

FLOW CHART 1: OUTLINE OF THE CALIBRATION AND MEASUREMENT HIERARCHY IN LABORATORY MEDICINE, JCTLM DB WG P-00 QUALITY POLICY



National Metroloy Institutes having CMCs listed in the BIPM KCDB according to CIPM MRA may also act as Reference Measurement Service providers; They will be listed by JCTLM according to the review process described in the document DBWG P-03B1

A calibration laboratory applying for listing on the JCTLM database as a Reference Measurement Service has to fulfill three different requirements (see FLOW CHART 2):

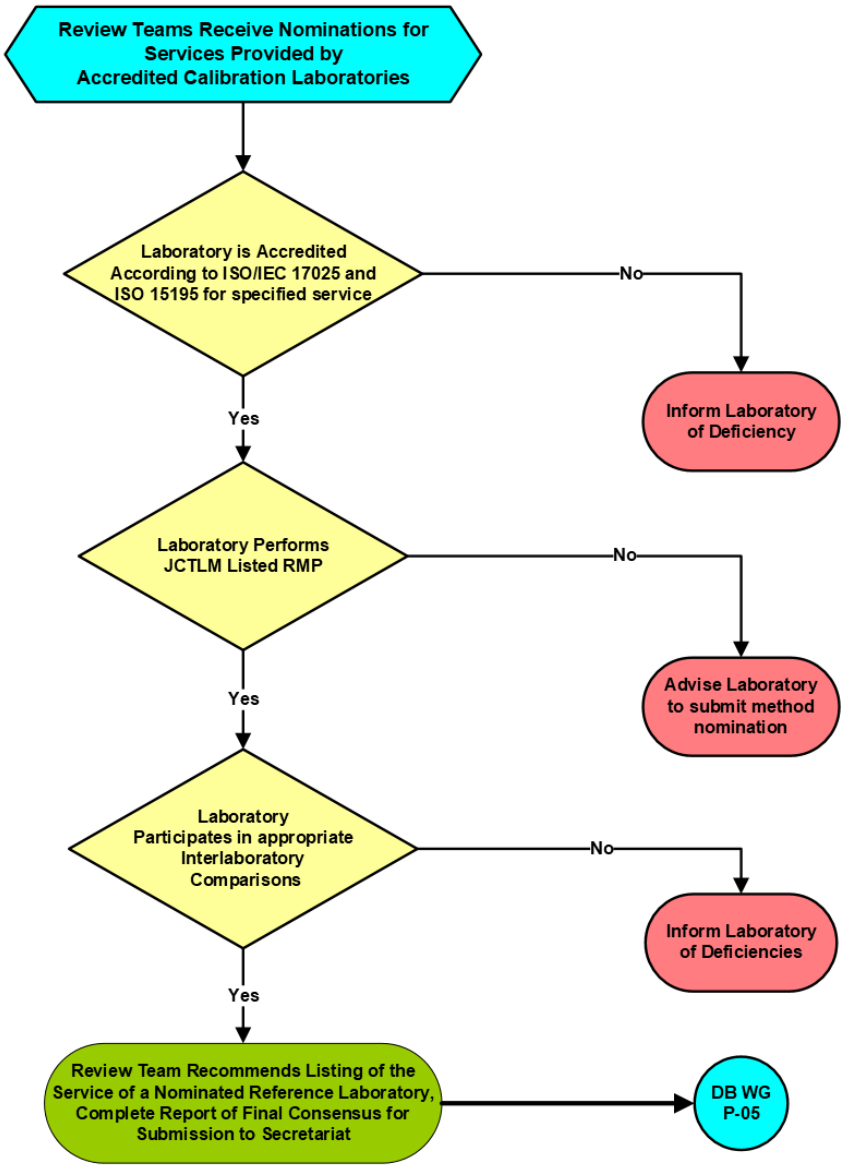
- accreditation according to ISO/IEC 17025 and ISO 15195,
- use of a RMP listed by the JCTLM database,
- participation in an External Quality Assessment Scheme (EQAS) dedicated to calibration laboratories.

Since 2003, IFCC provides an EQA scheme in order to support the activities of the JCTLM.

FLOW CHART 2: PROCESS FOR REVIEW OF REFERENCE MEASUREMENT SERVICES FROM LABORATORIES WHO ARE ACCREDITED AS CALIBRATION LABORATORIES, DB WG P-03-B2

PROCESS FOR REVIEW OF REFERENCE MEASUREMENT SERVICES FROM LABORATORIES WHO ARE ACCREDITED AS CALIBRATION LABORATORIES (ISO-17025/ 15195)
DB WG P-03-B2

Responsibility: JCTLM Review Teams



3. Scope

The scope of the IFCC External Quality Assessment Scheme (RELA) is to enable calibration laboratories and candidate calibration laboratories to demonstrate their competence through regular participation in surveys.

The survey results may be also used to demonstrate equivalence or discordance of different reference measurement procedures.

4. Procedures for Conducting the RELA surveys

4.1. The **IFCC Survey for Calibration Laboratories (RELA)** is organized on behalf of the IFCC by the Reference Institute for Bioanalytics (RfB) of the Foundation for Pathobiochemistry and Molecular Diagnostics. This foundation was created by the German Society for Clinical Chemistry and Laboratory Medicine (DGKL).

4.2. The Committee of Traceability in Laboratory Medicine (C-TLM) is the scientific advisory board of RELA.

4.3. Surveys are conducted **annually**; they are announced on the RfB website (https://www.dgkl-rfb.de/index.shtml).

4.4. Surveys are offered for several groups of **measurands**:

- Metabolites & Substrates,
- Electrolytes,
- Enzymes,
- Glycated hemoglobins,
- Proteins,
- Hormones,
- Thyroid hormones,
- Therapeutic drugs,
- Vitamins,
- Hemoglobin

4.5. **Key measurands** are selected for each group of measurands in each survey to collect statistically significant sample numbers. The selected key measurand for each group of measurands will change from one survey to the next.

Example:

The EQAS organization will offer surveys for all enzyme activity measurements according to the IFCC 37 °C reference measurement procedures. Due to the considerable workload, not all laboratories will participate for all measurands. At the worst, Lab A will analyze enzyme A, Lab B will analyze enzyme B, Lab C will analyze will analyze enzyme C, etc. Because of the limited number of participating laboratories, it will then be difficult to collect a statistically relevant number of results for each of the measurands necessary to demonstrate comparability of results from different laboratories. Therefore, the EQAS organizer will select one key measurand from each group of measurands for every survey occasion. It is recommended to provide results for this key measurand. Participation for all other measurands is voluntary.

4.6. It is generally expected that calibration laboratories apply **RMPs according to ISO 15193 and listed in the JCTLM database**. However, **candidate calibration laboratories** which are investigating a new analytical principle for establishing a reference procedure are also invited to validate their procedures by participation in the surveys. **Results from laboratories that obviously perform routine procedures will be excluded from the evaluations.**

4.7. In order to participate, laboratories need to **register** on the RfB website (https://www.dgkl-rfb.de/index.shtml). After registration the laboratories need to log in to their account where they need to submit an order for which measurands they want to participate in the upcoming survey. Key measurands are expressively labeled in bold. Registration needs to be done only once. Order of measurands has to be placed for every survey.

4.8. For each measurand**, two samples** with different concentrations/catalytic activity concentrations will be distributed to the participants.

4.9. It is expected that the results be established in the manner the participating laboratory usually employs when providing reference measurements for a customer. Therefore, an **appropriate number of vials** will be sent to the participants in order to enable replicate measurements necessary for the estimate of measurement uncertainty according to GUM.

4.10. **A dead-line** for reporting results will be set at six months after distribution of samples.

4.11. Participants are requested to report **information on their results** (e. g. mean values and expanded measurement uncertainties) as well as the RMP applied.

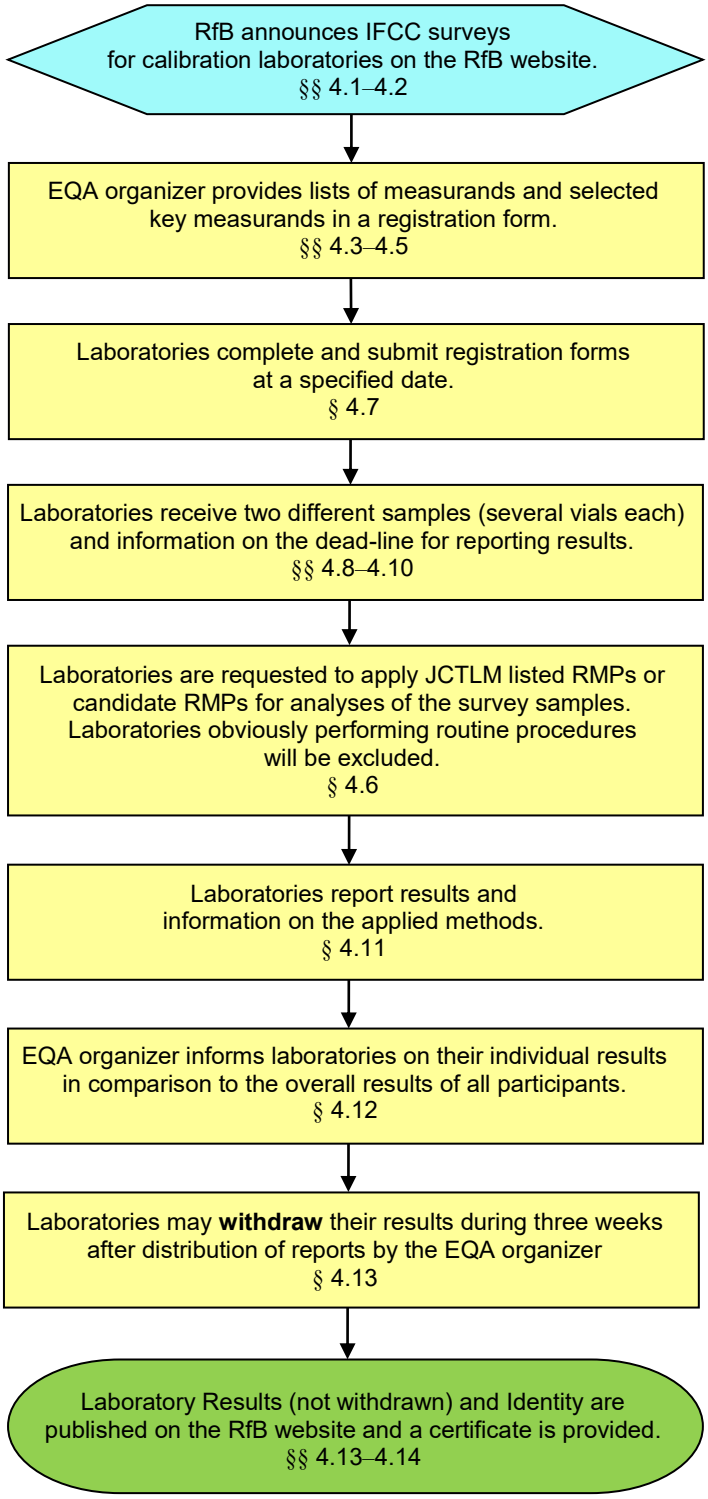
4.12. Participants will receive the **individual results** for each ordered measurand in comparison to the **overall results** of all participating laboratories for that measurand in a tabulated form as well as a **Youden diagram**.
In addition, Educational median ranges (EMR) are displayed in the Youden diagram. These ranges are not considered as a "grading" system. They are of no regulatory impact but may be used for educational means to improve laboratory performance. The EMR are set by the C-TLM (see Appendix 1). Results of at least five participants using a JCTLM listed RMP must be available so that the median and the EMR can be calculated on a valid statistical basis.

4.13. Participants may **withdraw** their results **within three weeks** after the first report has been distributed to the individual laboratories. Thereafter, all results (not withdrawn) including information on the identity of the laboratories will be made publicly available on the RfB website (https://www.dgkl-rfb.de/index.shtml).

4.14. Participants will also receive a **certificate of participation** indicating the measurands for which results were published.

4.15. **Participants are charged a fee to cover the expenses** for transport and materials. The costs are calculated on a non-profit basis.

FLOW CHART 3: PROCESS FOR CONDUCTING IFCC SURVEYS FOR CALIBRATION LABORATORIES



5. Related documents

5.1. BIPM, *The International System of Units (SI)*, 9th edition, Paris, France (2022), https://www.bipm.org/en/publications/si-brochure.

5.2. JCTLM, *The JCTLM Framework* (Appendix IV of the Declaration of Cooperation between the BIPM, IFCC and ILAC for the Operation of the Joint Committee for Traceability in Laboratory Medicine, 2019).

5.3. JCGM, International vocabulary of metrology – Basic and general concepts and associated terms (VIM), 3rd edition, Paris, France (2012), https://www.bipm.org/en/committees/jc/jcgm/publications.

5.4. ISO/IEC 17025: *General requirements for the competence of testing and calibration laboratories*, ISO, Geneva, Switzerland (2017).

5.5. ISO 15195: *Laboratory medicine Requirements for the competence of calibration laboratories using reference measurement procedures*, ISO, Geneva, Switzerland (2018).

5.6. ISO 15193: *In vitro diagnostic medical devices – Requirements for reference measurements procedures*, ISO, Geneva, Switzerland (2009).

5.7. ISO 15194: *In vitro diagnostic medical devices — Measurement of quantities in samples of biological origin — Requirements for certified reference materials and the content of supporting documentation*, ISO, Geneva, Switzerland, (2009).

5.8. ISO 17511*: In vitro diagnostic medical devices — Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples*, ISO, Geneva, Switzerland (2020).

5.9. IVDR: Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU, https://euivdr.com.

5.10. JCTLM DB WG, *Outline of JCTLM procedures for service nomination review*, JCTLM-DBWG/P-01B.

5.11. JCTLM DB WG, *Nomination process for reference measurement laboratory services*, JCTLM-DBWG/P-02B.

5.12. JCTLM DB WG, *Review of measurement services from accredited laboratories*, JCTLM-DBWG/P-03 B2.

6. Acronyms

BIPM:	International Bureau of Weights and Measures, https://www.bipm.org
CIPM:	International Committee for Weights and Measures, https://www.bipm.org/en/committees/ci/cipm
CMC:	Calibration and Measurement Capability
C-TLM:	IFCC Committee on Traceability in Laboratory Medicine, https://ifcc.org/ifcc-scientific-division/sd-committees/c-tlm/
EMR:	Educational median range
EQAS:	External Quality Assessment Scheme
GUM:	Evaluation of measurement data — Guide to the expression of uncertainty in measurement
ICSH:	International Council for Standardization in Haematology, https://www.icsh.org
IFCC:	International Federation of Clinical Chemistry and Laboratory Medicine, https://ifcc.org
ILAC:	International Laboratory Accreditation Cooperation, https://ilac.org
ISO	International Organization for Standardization, https://www.iso.org
JCGM:	Joint Committee for Guides in Metrology, https://www.bipm.org/en/committees/jc/jcgm
JCTLM:	Joint Committee for Traceability in Laboratory Medicine, https://jctlm.org
JCTLM DB WG:	JCTLM Database Working Group, https://www.bipm.org/en/committees/jc/jctlm/wg/jctlm-dbwg
RMP:	Reference Measurement Procedure
RfB:	Reference Institute for Bioanalytics, www.rfb.bio/cgi/switchLang?lang=en
VIM:	International Vocabulary of Metrology – Basic and general concepts and associated terms

7. Definitions

Analyte:	Component represented in the name of a measurable quantity [ISO 17511:2020].
JCTLM database:	The JCTLM Database lists higher-order reference materials, measurement methods and services to be used in calibration hierarchies for value assigning calibrators and trueness control materials for quantities measured by in vitro diagnostic medical devices. The listed reference materials, measurement methods and services when applied following the models described in ISO 17511:2020, 'In vitro diagnostic medical devices — Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples', can be used to establish metrological traceability. Database entries have undergone independent review and found to be compliant with the criteria in documentary standards developed by ISO TC 212 WG2 (Reference Measurement Systems), with reference measurements services listed for accredited calibration laboratories, as described in the JCTLM procedures [www.jctlmdb.org, accessed 08/20/2024]
Measurand:	Quantity, intended to be measured [VIM, 3rd edition, JCGM 200:2012].
Quantity:	Property of a phenomenon, body, or substance, where the property has a magnitude that can be expressed as a number and a reference [VIM, 3rd edition, JCGM 200:2012].
Uncertainty (of measurement):	Non-negative parameter characterizing the dispersion of the quantity values being attributed to a measurand, based on the information used [VIM, 3rd edition, JCGM 200:2012]. Methods for calculation must be specified.

8. Revision History

Version number	Date of Issue/Review	Summary of change
1.0	05/20/2005	Draft Issue for IFCC C-TLM
1.1	08/02/2005	
1.2	10/01/2008	4.11 is modified (‘limits of equivalence’), Appendix 1 is added
1.3	07/04/2008	
1.4	11/01/2024	Revision of: measurands offered, links, Appendix 1, Related documents, Acronyms, Flow chart figures, Rename LoE to EMR

9. Appendix 1

In Table 1 all Educational median ranges EMR for measurands offered in RELA surveys are listed. This list has to be supplemented as soon as new measurands are introduced. The EMR do not represent a tolerance limit for passing or not. They just have educational character for orientation.

TABLE 1: MEASURANDS, CORRESPONDING EDUCATIONAL MEDIAN RANGES

Group	**Analyte**	**EMR / %**
Metabolites and Substrates (META)	Total Cholesterol	± 3.25
	Total Glycerol	± 4.0
	Creatinine	± 5.00
	Uric Acid	± 3.25
	Urea	± 5.00
	Glucose	± 3.75
	Total Bilirubin	± 5.50
Electrolytes (ELEC)	Sodium	±1.25
	Potassium	± 2.00
	Chloride	± 2.00
	Calcium	± 2.50
	Lithium	± 3.00
	Magnesium	± 3.75
Enzymes (ENZY)	Alanine aminotransferase (ALT)	± 5.25
	Aspartate transferase (AST)	± 5.25
	Creatine kinase (CK)	± 5.00
	Lactate dehydrogenase (LDH)	± 4.50
	Glutamyl transferase (GGT)	± 5.25
	Total Amylase	± 5.25
	Pancreatic Amylase	To be determined

Group	**Analyte**	**EMR / %**
Glycated Hemoglobin (GLYC)	HbA1c	± 4.50
Hemoglobin (HEMO)	Total hemoglobin	± 1.50
Proteins (PROT)	Total proteins	± 2.50
Vitamins (VITA)	25-OH-vitamin D3	± 7.50
Hormones (HORM)	Aldosterone	± 8.75
	Cortisol	± 7.50
	Progesterone	± 8.75
	Testosterone	± 8.75
	Estradiol-17β	± 8.75
	Estriol	± 7.50
Thyroid Hormones	Total Thyroxine	± 6.00
	Total Triiodothyronine	± 6.00
	17-OH-Progesterone	± 7.50
Therapeutic drugs (THER)	Digoxin	± 7.50
	Digitoxin	± 7.50
	Theophylline	± 6.00
	Valproic acid	± 5.00