

QUALITY MANUAL: MODEL ACCORDING EC4 ESSENTIAL CRITERIA v.2.0

9. POST-ANALYTICAL PHASE

9.4. REFERENCE VALUES

AUTHOR	VERSION	APPROVED BY	DATE	

CIRCULATION LIST:	NAME	POSITION

CODE) DOCUMENT: QMM09	(CHAPTER TITLE):	(INSTITUTION): EC4 UNIVERSITY HOSPITAL
(CODE) SECTION: QMM09-S04	POST-ANALYTICAL PHASE	EC4 CLINICAL CHEMISTRY DEPARTMENT
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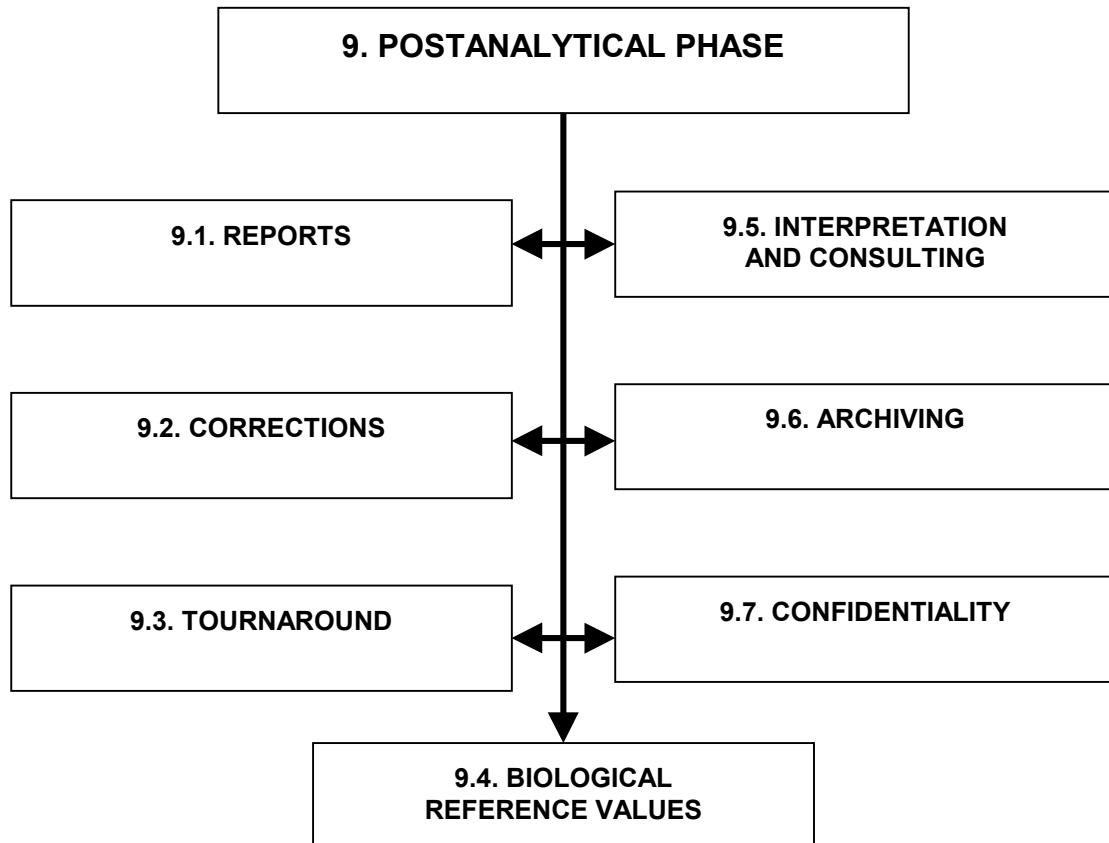
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1. INTRODUCTION

Reference values should be available for all assays, where relevant.

The reference values should be checked by the laboratory.

1.1. SCOPE



1.2. AIMS

To fulfil the requirements of the following clauses:

ISO 15189	ISO 9000: 2000	ISO 17025
5.5. Examination procedures. 5.3.3.. – 5.5.5.		
5.8. Reporting results. 5.8.3.		
B.5.2., B.6.2.		

1.3. PUBLICATION CREDITS

EC4 WG

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1.4. REFERENCES

1. Jansen RTP, Blaton, V, Burnett D, Huismann W, Queraltó JM, Zérah S, Allman B. European Communities Confederation of Clinical Chemistry. Essential criteria for quality systems of medical laboratories. Eur J Clin Chem Clin Biochem 1997; 35(2): 123-132.
2. ISO/DIS 15189 – Quality management in the medical laboratory (December 1998). 5.5.6 i 5.8.2.
3. ISO, IEC. General requirements for the competence of calibration and testing and calibration laboratories. DIS 17025. Geneva: ISO, 1998. 5.4., 5.10.
4. ISO.DIS Quality management systems – Requirements. ISO 9000. Geneva: ISO, 2000., 7.2.1., 7.5.5.
5. Solberg HE. Establishment and use of reference values. A: Burtis, C. A., Ashwood, E. R., eds: Tietz Textbook of Clinical Chemistry. Philadelphia, PA: W.B. Saunders Co, 1999.
6. Jansen RTP, Bank CMC, Huisman W, Penders TJ. NVKC Model quality manual. 2nd rev. Ed. Utrecht: NVKC 1996.

1.5. RELATED DOCUMENTS

QM 07-03. Pre analytical phase. Repertoire

QM 09-01 Post analytical phase. Reporting procedures. Report form.

MPD 0202-0-0701. Laboratory user's handbook.

MPD 0202-0-0941 Procedure for obtaining reference values

MPD 0202-0-0942 Procedure for reference values transferability

MPD 0202-0-0943 Procedure for adopting reference values

MPD 0202-0-0944 Biological reference values list

MPD 0202-0-0945 Critical results ("panic values") list

1.6. ABBREVIATIONS

LIS: Laboratory information system

1.7. RELATED DEFINITIONS

analyte: component indicated in the name of a measurable quantity. NOTE 1: Analyte and component are different concepts from measurable quantity and measurand which furthermore require indication of system and kind-of-quantity. NOTE 2: The term analyte has also been used specifically for the component of a solution applied to the sensor of a measuring system and providing the output signal. This component may not be identical to that of the measurand.

biological reference value: value of a measurand in an individual belonging to a defined reference sample group of individuals. NOTE 1 Reference values may have to be classified according to factors of influence such as the diurnal variation, sex, race, or age of the population studied. When applicable, a distribution of values is expressed in term of reference limits (upper and lower). The source of material upon which they are based and the procedure for their determination should be documented. NOTE 2 A biological reference interval usually refers to the central 95-percentile of the distribution of reference values.

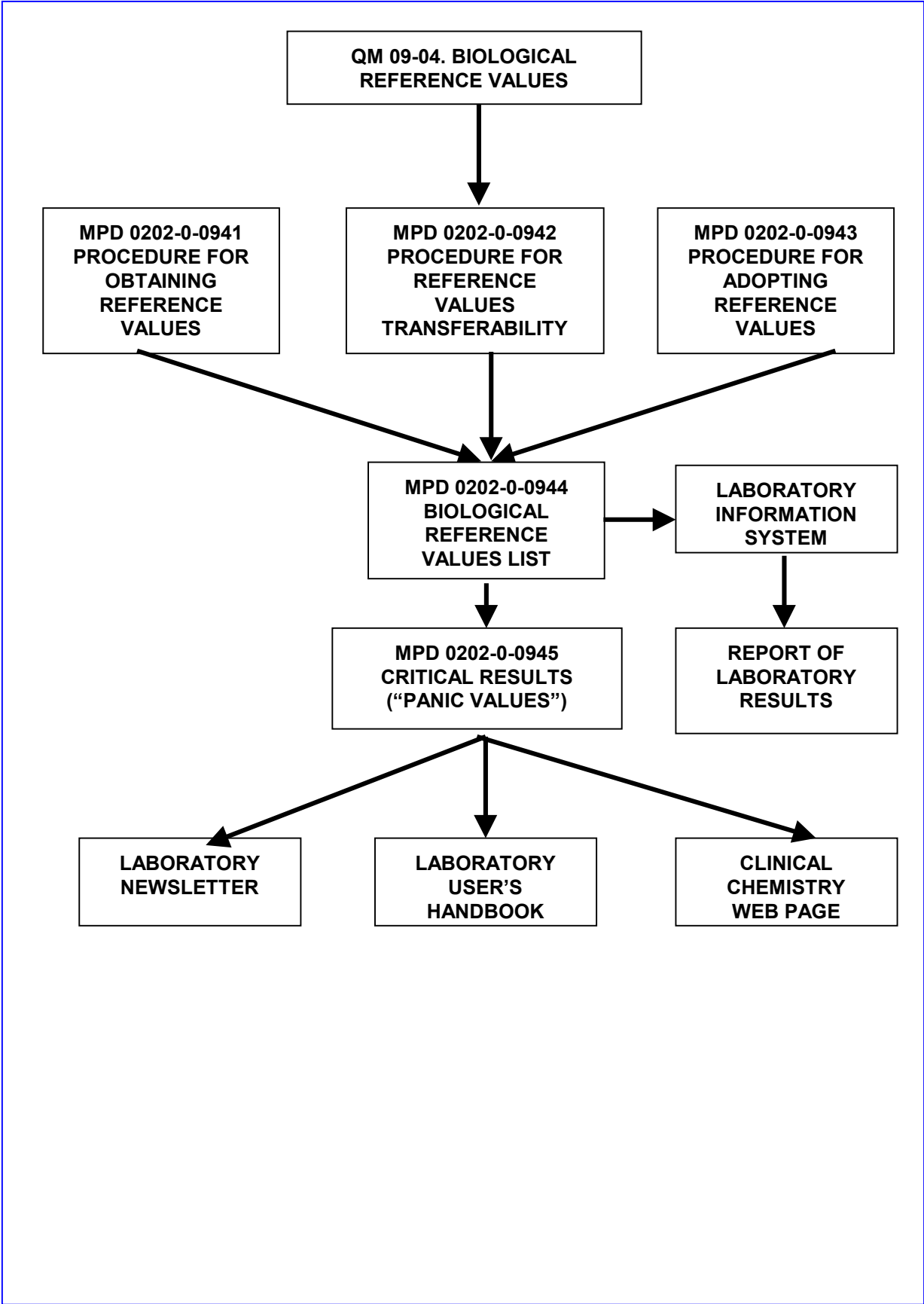
interval: set of all values lying between and sometimes including one or both of the lower limiting value and higher limiting value. NOTE 1: If both limits are excluded, the interval is open; if both are included, it is closed. NOTE 2: The definition given corresponds to a statistical usage, e. g. confidence interval and statistical coverage interval. In general metrology, interval is also used to mean the difference between the higher and the lower limiting values, whereas the set is called "range", e. g. range of indication.

central 0,95 - interfractile interval: closed interval of values between the 0,025- and 0,975-fractiles of a set of values. NOTE: If the limits are derived from a sample of values, the employed type of non-parametric or parametric statistics should be indicated.

report of measurement: document that presents the name of the measurand, and result of measurement, together with an expression of the uncertainty of measurement, the values of relevant influence quantities, information necessary for the identification of the sample, the requester, and the organisation or laboratory issuing the report, and sometimes interpretative remarks.

result of a measurement: value attributed to a measurand, obtained by measurement. NOTE 1: When the term result of a measurement is used, it should be made clear whether it refers to (a) the uncorrected result of a measurement; (b) the corrected result of a measurement; (c) a single observation or an average of the values obtained by several observations. NOTE 2: A complete statement of the result of a measurement includes information about the uncertainty of measurement and about the values of relevant influence quantities.

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2. OBTENTION OF BIOLOGICAL REFERENCE VALUES

According to the IFCC recommendations, reference values are defined as the central interval which includes 95% of the statistical distribution of results observed in a sample (reference sample) randomly selected from a (reference) population of reference individuals. The health status of these individuals is well defined.

In the Clinical Chemistry Department, the biological reference values are obtained:

- in (healthy) reference individuals from a Reference population, as it is established in international recommendations
- from peer reviewed literature, when the procedure follows the international recommendations
- from the manufacturer, provided the method used follows the international recommendations

The *Laboratory User's Handbook* includes a list of all reference intervals, the partition group, and their source. The procedures *MPD 0202-0-0941. Procedure for obtaining reference values*, *MPD 0202-0-0942 Procedure for reference values transferability*, and *MPD 0202-0-0943 Procedure for adopting reference values*, following strictly the IFCC recommendations, contains the production details when biological reference values are produced in the Clinical Chemistry Department.

3. EXPRESSION OF BIOLOGICAL REFERENCE VALUES

The reference values, when appropriated, are:

- printed in each report, as displayed in the document *QM 09-01 Post analytical phase. Reporting procedures. Report form.*;
- appears in the *Laboratory user's handbook* (both in electronic and printed versions);
- printed in a special issue of the *Laboratory Newsletter*;
- appears in the Clinical Chemistry Department Web.

The *Laboratory user's handbook* presents this information as:

Laboratory user's handbook

Biological reference values

Analyte	Main group	Other groups	Biological reference interval* (units)	Production
Serum Potassium	1d -4w 2-12 m 0-1 y Adult		3.6-6.1 mmol/L 3.6-5.8 mmol/L 3.1-5.1 mmol/L 3.5-5.1 mmol/L	Clinical Chemistry Laboratory, technical report 1996; TRDCC 12.
Serum Urate	1-4 w 0-6 m 7m-1y Adults	W M	<311 µmol/L <372 µmol/L <362 µmol/L <340 µmol/L <320 µmol/L	Manufacturer, 1988
Serum Protein	Adults		63-83 g/L	Tietz NW. Clinical guide to laboratory tests, 2 nd ed. Philadelphia: WB Saunders, 1990

(*) 0.95 inter-fractile interval

4. THERAPEUTIC INTERVAL

In therapeutic drug monitoring a similar (but completely different) concept is the therapeutic interval. This interval includes the plasma concentrations which in the vast majority of patients there is beneficial effects without toxicity.

Therapeutic ranges, when appropriated, are:

- printed in each report, as displayed in the document *QM 09-01 Post analytical phase. Reporting procedures. Report form.*;
- appears in the *Laboratory user's handbook* (both in electronic and printed versions);
- printed in a special issue of the *Laboratory Newsletter*;

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(d) appears in the Clinical Chemistry Department Web.

The *Laboratory user's handbook* present this information as:

Laboratory user's handbook

Therapeutic Ranges

Drug	Group	Therapeutic range**(units)	Production
Serum Digoxin		0.5-2.0 nmol/L	Clinical Chemistry Department, report not published, 1992
Serum Phenytoin	Premature infants Adults	24-56 µmol/L 20-80 µmol/L	Manufacturer, 1996

(**) Range not formally established

5. TOXICOLOGY

Toxicology information, when appropriated, is:

- (a) printed in each report, as displayed in the document *QM 09-01 Post analytical phase. Reporting procedures. Report form.*;
- (b) appears in the *Laboratory user's handbook* (both in electronic and printed versions);
- (c) printed in a special issue of the *Laboratory News/letter*;
- (d) appears in the Clinical Chemistry Department Web.

The *Laboratory user's handbook* present this information as:

Laboratory user's handbook

Toxicology information

Substance	Main group	Other groups	Biological reference values (units)	Production
Serum Aluminium			<15 µg/L	Referral laboratory, 1998
Urine Cadmium	Exposed		<5 µg/g creatinine	Smith A, Weson B. Clin Chem Acad J., 1993: 1: 2-3.
Whole blood Lead	Adults	W M	<0.41 µmol/L <0.48 µmol/L	Burtis CA, Ashwood ER. Tietz N. Textbook of Clinical Chemistry, 2 nd ed. Philadelphia: WB Saunders, 1994

6. CRITICAL VALUES (“PANIC VALUES”)

For each type of test, the Clinical Chemistry Department defines a range outside which results have to be marked with a warning sign. Where possible, these warning mechanisms are incorporated into the software of automatic laboratory equipment or the LIS.

A complete list of the “panic” values is included in the procedure *MPD 0202-0-0945 Critical results (“panic values”) list*.

7. TRACEABILITY OF BIOLOGICAL REFERENCE VALUES AND CRITICAL (“PANIC”) VALUES

Following the IFCC guidelines, the Clinical Chemistry Department produce his own biological reference values, when possible. The procedure used is inspired in the IFCC (and other authority organizations) guidelines. When it is not possible the production in the laboratory, biological reference ranges will be adopted from reliable sources, quoted in the printed expression.

8. RESPONSABILITIES ON “REFERENCE VALUES”

The production, maintenance and revision of documents concerning the production, expression and traceability of biological reference values documents is a duty of the head of each area of the Clinical Chemistry Department.

The compilation and diffusion of the biological reference list is a duty of the Quality Officer.

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9. DOCUMENT MANAGEMENT

Updated documents concerning the biological reference are available in the document volume of the LIS.

One copy of these procedures is kept in the Quality System Files. Staff members of the Clinical Chemistry Department receive an update copy as soon as it is available.

All the clinical staff of the parent institution are provided with copies of the reference and critical values.

10. REVIEW OF DOCUMENTS

Documents concerning the interpretation and consulting activities are revised at least twice in a year.

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