WORK INSTRUCTION

QUALITY CONTROL PROCEDURES IN CHEMICAL PATHOLOGY

HSA/JP/CP/WI-002

CHEMICAL PATHOLOGY UNIT
DEPARTMENT OF PATHOLOGY
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CONTROLLED DOCUMENT
VERSION NO: 1
DATE OF ISSUE: 1 MAC 2021

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AMENDMENT

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1.0 OBJECTIVE

Implementation of Internal and External Quality Control and to ensure the laboratory performance is acceptable.

2.0 SCOPE

This document provides a summary of all process of establishing and maintaining a quality control for quantitative tests that is practiced in Chemical Pathology laboratory.

3.0 REFERENCE

- Assuring The Right Quality Right , James O.Westgard, Ph.D.,F.A.C.B
- A Multi- rules Shewhart Chart for Quality Control in Clinical Chemistry. J.O Westgard et. al. Clin.Chem.27,493-501(1981).
- International Standard MS ISO 15189:2014 Medical Laboratories Requirement for quality and competence.

4.0 DEFINITION AND ABBREVIATION

4.1 DEFINITION:

4.1.1 Analytical run (R)

In laboratory operations, control samples are analyzed during each analytical run to evaluate method performance; therefore the analytical run defines the interval (period of time or number of specimens) between evaluations of control results.

4.1.2 Control rules

Rules set up by the laboratory to identify whether the quantitative results of the control material are out of control.

4.1.3 Accuracy

Closeness of the agreement between the result of a measurement and a true value of the measurand.

4.1.4 Precision

Closeness of agreement between quantity values obtained by replicate measurements of a quantity, under specified conditions.

4.1.5 Mean

The arithmetic average of a group of values. This is determined by summing the values and dividing by the number of values.

4.1.6 Standard Deviation

A statistic which describes the dispersion about the mean. The standard deviation is related to the width of a normal curve.

4.1.7 Range

Range refers to the difference or spread between the highest and lowest observations.It is the simplest measure of dispersion.

4.1.8 Total Error

Total error is defined as the total allowable difference from the accepted reference value seen in the deviation of a single measurement from the target value. Total Error limits can be defined by medical usefulness or by external proficiency testing criteria such as the RCPA or CAP, biologic specifications for imprecision and accuracy and the US CLIA criteria for Total Error.

4.1.9 Random Error

Random Error is defined as the dispersion of independent test results obtained under specified conditions. It is expressed as the maximum allowable coefficient of variation (CV%) of the results in a set of replicate measurements.

4.1.10 Systematic Error

Systematic Error is defined as the expressed difference between the average result obtained by a procedure under specified conditions and an accepted reference value or the deviation of the mean from the target value. Bias is expressed as the maximum allowable difference (Delta diff) of an average result in a set of replicate measurements and its expected reference value.

4.1.11 Trend

A trend is a sustained increase or decrease in a quality control value over a period of four or more days with the latest value at or beyond the 2 SD limits. If no action is taken, the QC limit may be breached.

4.1.12 Shift

A shift is a sudden change in the mean value of the accumulated quality control values. Precision is not affected but the plotted points stay consistently to one side or the other of the calculated mean value, indicating a shift in the distribution of control values with a new mean.

4.1.13 Drift

A drift is a gradual change of more than one set of controls that show a shift between the beginning and end of a run in the same direction.

4.1.14 Calibrator

A solution which has a known amount of analyte weighed in or has a value determined by repetitive testing using a reference or definitive test method.

4.1.15 Control

Material or preparation used to monitor the stability of the test system within predetermined limits.

4.1.16 Independent (Third-Party) Control

QC materials that are independent of the calibration materials or obtained from a different supplier of the analyzing system.

4.1.17 Quality Control

Quality control in the medical laboratory is a statistical process used to monitor and evaluate the analytical process that produces patient results.There are two types of quality control is being performed in laboratory:-

a) Internal Quality Control

Is a statistical process used to monitor and evaluate the analytical process that produces patient results.

b) External Quality Control

The primary aim of proficiency testing is to provide quality assurance tool for individual laboratories to enable them to compare their performance with similar laboratories, to take any necessary remedial action, and to facilitate improvement. Example: EQAS,RCPA and RIQAS.

4.2 ABBREVIATION:

MLT	:	Medical Laboratories Technologist
QC	:	Quality Control
IQC	:	Internal Quality Control
LIS	:	Laboratory Information System
EQAS	:	External Quality Assurance Scheme
RIQAS	:	Randox International Quality Assurance Scheme
SD	:	Standard Deviation
CV	:	Coefficient of Variation
RT	:	Room Temperature
EQA	:	External Quality Assurance

5.0 PROCEDURE

5.1 Implementation Quality Control

5.1.1 Properties of QC Material

a) The material matrix resembles a human sample and is commutable (blood, plasma, serum, CSF,and/or urine).

b) The analytes concentration should be at medically significant levels. It should span the clinically important range of analytes concentration.

c) The control material should be tested in the same manner as patient specimens.

d) Minimum two levels should be tested each time.

e) Control material obtain preferably be “third party”

f) The open vial of QC material must be stable according to the usage of laboratory.

Refer to Appendix 1 for the list of internal quality control material providers for each analytes.

5.1.2 Storage of QC Material

a) The storage criteria of QC material, shall comply with the recommendation by the supplier. Please follow the instruction in “QC package insert” which came together with QC material purchased.

b) All QC material received from the vendor must be packaged and delivered to the laboratory following the delivery specification. Expired and short expiry quality controls are not accepted.

Refer to QC package insert for details.

5.1.3 QC Material Preparation

Preparation QC material:

a) Serum/Urine (Liquid) refer to Appendix 2a: QC Preparation Flow Chart for Liquid (serum /urine)

b) Dry Powder (Lypholysed) refer to Appendix 2b: QC Preparation Flow Chart (Lypholysed) for Dry Powder

5.2 Internal Quality Control

5.2.1 Establishment & Implementation

a) Analyse the control materials to obtain a minimum of 20 measurements over a 20 days period under laboratory's own operating conditions. Use QC manufacturer claim reference as guidance.

b) Calculate the mean and standard deviation (SD) of the control measurements.

c) After 100 data or monthly review, the mean and SD is reviewed and recalculated when necessary.

d) Calculate the control limits for the control rules to be applied.
E.g. 2 SD Control Limit.
Upper Control Limit : Mean + 2(SD)
Lower Control Limit : Mean – 2 (SD)

e) Prepare control charts by entering the appropriate parameters in a computerized monitoring and charting package in a specific analyzer.

f) Use procedure as above for any changes in QC Lot. No. or test methods. The collection of data for the new IQC lot should start before the current IQC lot finishes at least 30 days prior.

5.2.2 Procedure

a) Analyse control materials after maintenance and at the beginning of analytical run, before proceeding with patient samples.

b) Review and interpret the control results to determine control status, as auto plot by software analyzer. Record the acceptance of QC results as follow format Appendix 3.

c) Continue to run the patient samples if none of the control rules for the respective tests were violated.

d) Determine the type of errors occurring (random, systematic or both) if control rules are violated.

e) Perform necessary corrective and troubleshooting action and record in the corrective action section in QC log book for each section.

f) Consult a supervisor or scientific officer if the problem is not resolved.

g) Review monthly QC LJ chart based on daily log;

i. CV monthly to inspect for any trend, small shift which indicate random error or imprecision that have been present.

ii. Bias monthly to monitor the changes in *systematic error* or *potential accuracy problems*

iii. Analyse any QC problems and discuss with relevant staff.

h)Check The Performance Of Each Analytes

1. Calculate Total Error test with % *bias* from External Quality Programme (EQA) and SD (% CV) from Internal Quality Control (IQC). Observe test status.

2. Every end cycle reports to be presented in Quality Meeting.(Refer File : *Laporan Pengurusan Kualiti Patologi Kimia)*

5.3 External Quality Control

5.3.1 Procedure

a) Receive control materials from suppliers. Refer to Appendix 4 : List of EQA providers for every participating analytes.

b) Analyse the control materials as patient samples and according to the instruction and schedule given.

c) Pass the analysed data to the QC officer.

d) Submit the report via online or Email to the respective organizer.

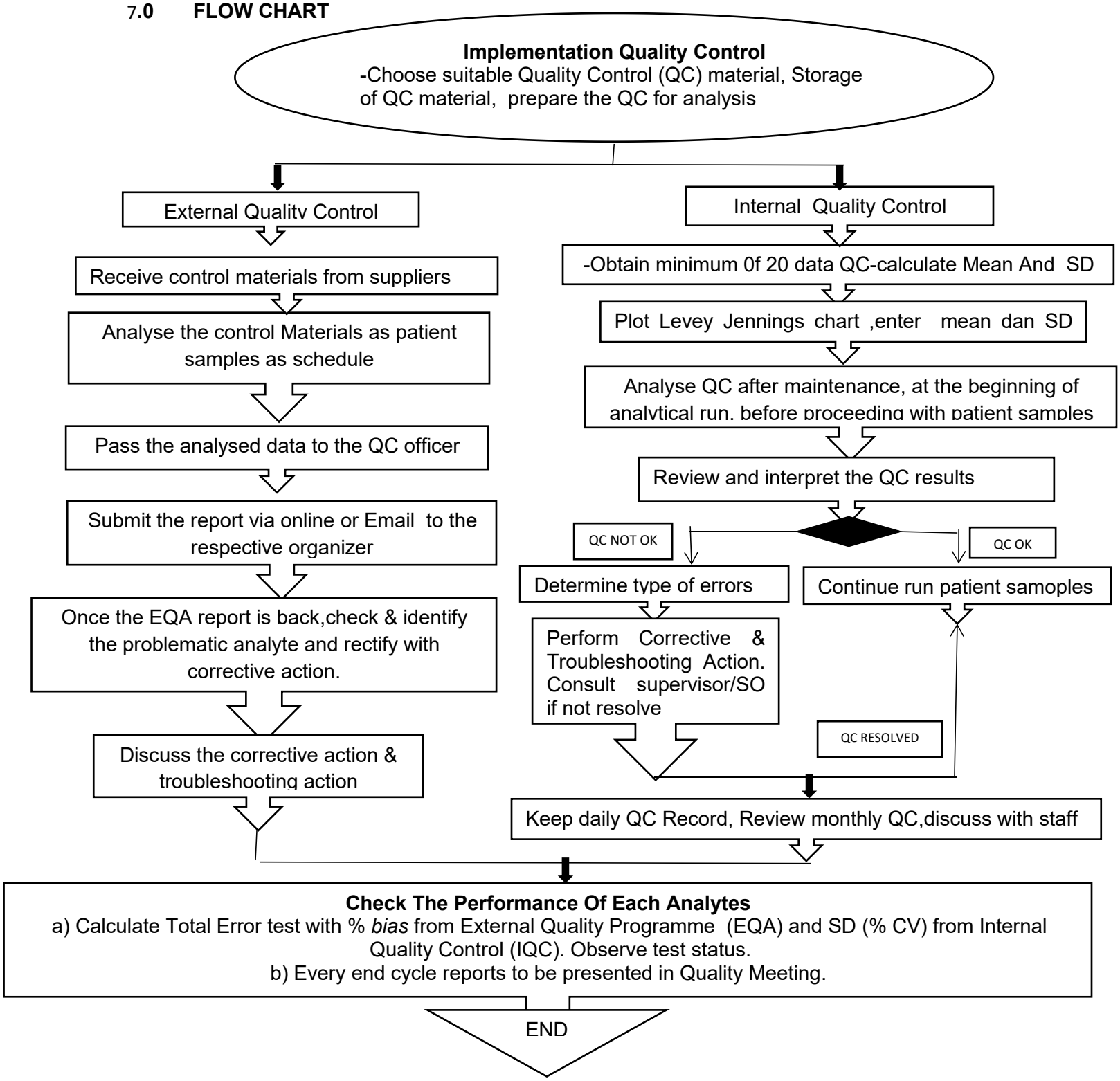
e) Once the EQA report is back,check and identify the problematic analytes and rectify with corrective action.

f) Discuss the corrective and troubleshooting action.

6.0 RECORDS

No	Record	Retention Time
1	External Quality Control files End Of Cycle Summary	5 years
2	Quality Control Data in LIS	3 years
3	Internal QC files	3 years
4	QC Material Preparation Manual (Package Insert) File	As long as the QC materials are used.
5	Remedial Action Log /QC Log Book	5 years

7.0 FLOW CHART



8.0 APPENDIX

NO	Appendix	
1	Appendix 1	List of internal quality control material providers for each analytes.
2	Appendix 2a	QC Preparation Flow Chart for Liquid (serum /urine)
3	Appendix 2b	QC Preparation Flow Chart (Lypholysed) for Dry Powder
4	Appendix 3a	Daily IQC Checking Format
5	Appendix 3b	*Borang Semakan Kawalan Kualiti Internal Mingguan*
6	Appendix 4	List of EQA providers for every participating analytes

Appendix 1

List of internal quality control material providers for each analytes

Type Of QC Inserts	Analytes	Unit
Liquichek™ Diabetes Control	HbA1C	%
Liquichek™ Immunology Control	Complement C3	g/L
	Complement C4	g/L
	C-Reactive Protein	mg/L
	Immunoglobulin A (IGA)	g/L
	Immunoglobulin G (IGG)	g/L
	Immunoglobulin M (IGM)	g/L
	Rheumatoid Factor (RF)	IU/mL
Liquichek™ Pediatric Control	Bilirubin (Direct)	umol/L
	Bilirubin (Total)	umol/L
Liquichek™ Urine Chemistry Control	Albumin	mg/L
	Amylase	U/L

Calcium	mmol/L
Chloride	mmol/L
Creatinine	umol/L
Glucose	mmol/L
Magnesium	mmol/L
Osmolality	mOSM/kg
Phosphate	mmol/L
Pottasium	mmol/L
Protein Total	g/L
Sodium	mmol/L
Urea	mmol/L
Uric Acid	mmol/L

Lyphochek® Assayed Chemistry Control	Albumin	g/L
	Alkaline Phosphatase	U/L
	ALT	U/L
	Amylase	U/L
	AST/SGOT	U/L
	Bilirubin (Direct)	mg/dL
	Bilirubin (Total)	Umol/L
	Calcium	mmol/L
	Chloride	mmol/L
	HDL	mmol/L
	Cholesterol (Total)	mmol/L
	Cholinesterase	kU/L
	Creatine Kinase	U/L
	Creatinine	mmol/L
	GGT	U/L
	Glucose	mmol/L
	Iron	Umol/L
	UIBC	Umol/L
	Lactic Acid	U/L
	Lactate Dehydrogenase	U/L
	Magnesium	mmol/L
	Osmolality	mOSM/kg
	Phosphorus	mmol/L

	Pottasium	mmol/L
	Protein Total	g/L
	Sodium	mmol/L
	Triglyceride	mmol/L
	Urea	mmol/L
	Uric Acid	Umol/L
Liquichek™Urine Toxicology Control, Level S1E Low Opiate, S2E Low Opiate	Morphine	ng/L
	Cannabinoid	ng/L
	Amphethamine	ng/L

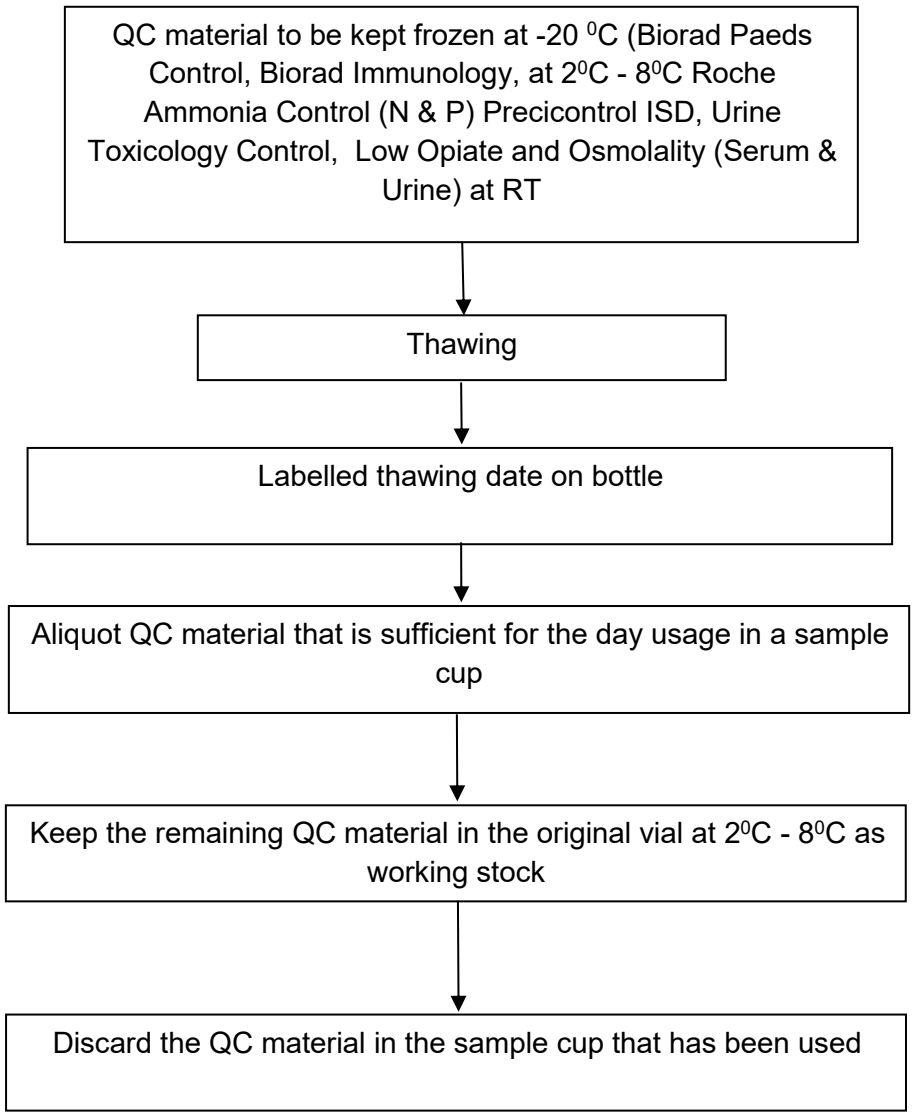
IQM	pH	
	pCO2	mm/Hg
	pO2	mm/Hg
Lypocheck Biorad Tumour Marker (lev 1,2,3)	AFP	ng/ml
	CA125	U/ml
	CEA	ng/ml
	TPSA	ug/l
Lypocheck Biorad Immunoassay Plus (Lev 1, 2, 3)	Cortisol	nmol/ml
	Ferritin	ng/ml
	Folate	nmol/ml
	FT3	pmol/l
	FT4	pmol/l
	FSH	mU/ml=IU/L
	BHCG	mU/ml=IU/L
	LH	mU/ml=IU/L
	Estradiol	pmol/l
	Progesterone	nmol/ml
	Prolactin	uU/ml=mIU/L
	Testosterone	nmol/ml
	TSH	uU/ml=mIU/L
	Vitamin B12	pmol/l

PreciControl Troponin	Troponin T High Sentivity	ng/L
Precicontrol Varia IPTH	IPTH	
Precicontrol Universal-Thyroglobulin		
Precicontrol ThyroAB-	Anti TG, Anti TPO	
Liquicheck Ethanol/ Ammonia Control	NH3	Umol/L
Biorad, Whole Blood Immunosuppressant (lev 1, lev 2, Lev 3)	Cylosporin, Tacrolimus	
PreciControl ISD (ISD I, ISD II & ISD III) (Backup)	Tacrolimus	ng/ml
PreciControl ISD (ISD I, ISD II & ISD III) (Backup)	Cyclosporin	ng/ml

Lypocheck Biorad Immunoassay Plus (Lev 1, 2, 3)	Acetaminophen	µg/ml
	Amikacin	µg/ml
	Carbamazepine	µg/ml
	Digoxin	ng/ml
	Gentamicin	µg/ml
	Phenobarbital	µg/ml
	Phenytoin	µg/ml
	Salicylate	µg/ml
	Theophylline	µg/ml
	Valporic acir	µg/ml
	Vancomycin	µg/ml
Ark Tm Methotrexate Control (Low, Med, High)	Methotrexate	

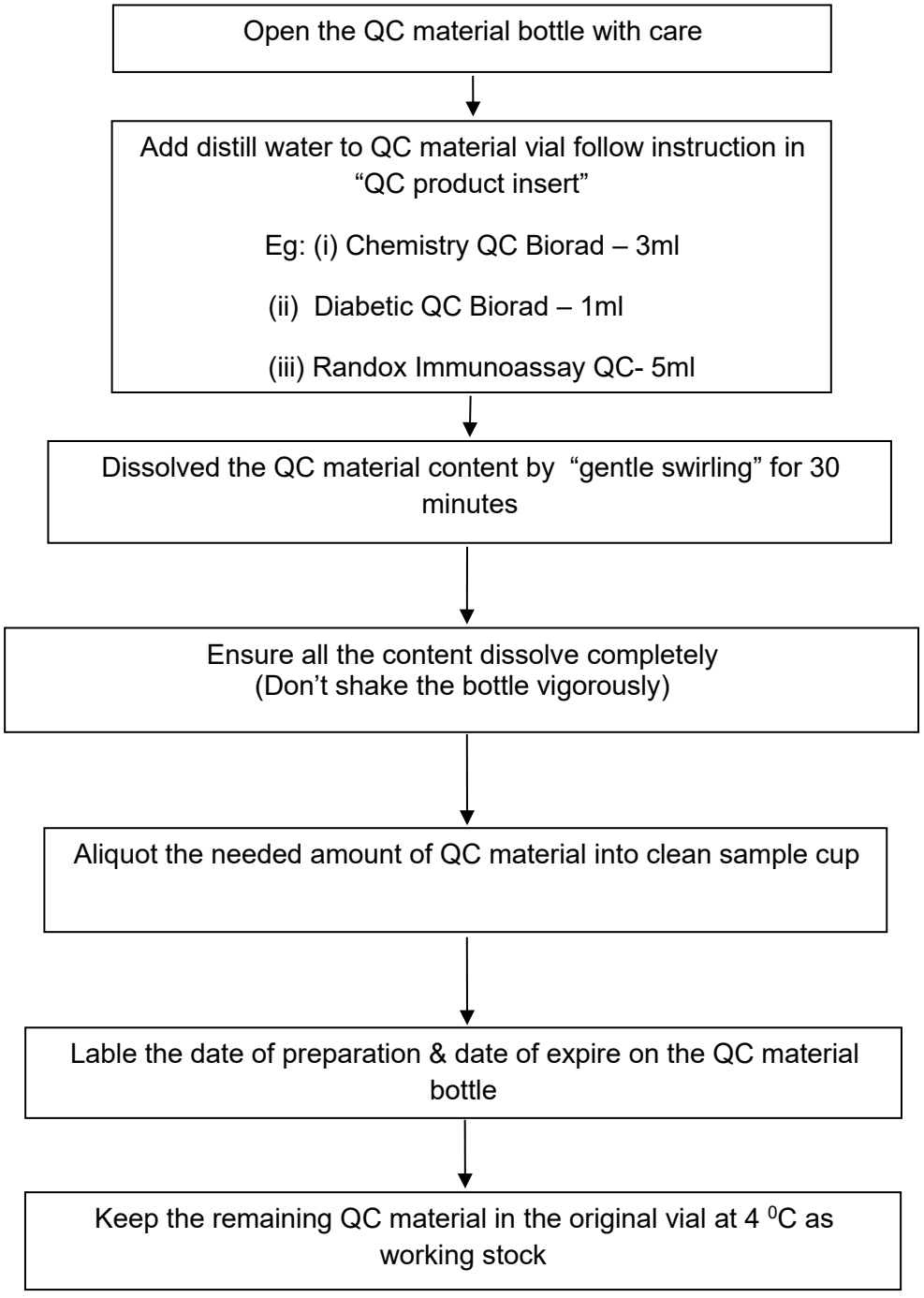
Appendix 2a

QC Preparation Flow Chart **(Liquid)**



Appendix 2b

QC Preparation Flow Chart **(Lypholysed)**



Appendix 3a

DAILY IQC CHECKING FORMAT

ANALYZER:

MONTH: YEAR:

NO	Test	Indicator: (√) IQC ACCEPTED (T) IQC ACCEPTED AFTER TROUBLESHOOTING (X) PROE (*) TRENDING																													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
1																																
2																																
3																																
Initial																																

Appendix 3b

Format On Weekly

BORANG SEMAKAN KAWALAN KUALITI INTERNAL MINGGUAN

ANALYZER:

PEGAWAI BERTUGAS:

BULAN: **TAHUN:**

BIL.	**UJIAN**		**PETUNJUK: (√) IQC DITERIMA (X) UJIAN BERMASALAH**				
		MINGGU:	1	2	3	4	5
		TARIKH:					
1							
2							
3							
TANDATANGAN:							
DISEMAK OLEH:							
TANDATANGAN:							

Appendix 4

CORRECTIVE & TROUBLESHOOTING ACTION FORMAT :

1. **DATE:**
2. **TIME:**
3. **ANALYTE:**
4. **LEVEL/CONCENTRATION:** LOW/NORMAL/HIGH/PEDIATRIC (L)/PEDIATRIC (H)
5. **MATERIAL (Name):**
6. **FLATFORM (Analyser):**
7. **PROBLEM:**

   ☐ 1_{2s}
   ☐ 2_{2s}within run
   ☐ 2_{2s} across run
   ☐ 1_{3s}
   ☐ 4s
   ☐ 4_{1s}
   ☐ 10x within material
   ☐ 10x across material

   ☐ Other……

8. **TROUBLE SHOOTING** (state order number in ☐ if more than 1 step done; e.g.insert number 1 in ☐ Recalibrate if recalibration was done as a first step in troubleshooting)

   ☐ Repeat run
   ☐ Change QC material
   ☐ Recalibrate
   ☐ Change reagent and calibrate
   ☐ Precision check
   ☐ Maintenance procedure: Specify:…….

   ☐ Identified hard ware problems: Specify:……

   ☐ Identified software problems: Specify:…….
   ☐ Call service engineer

9. CAUSED BY

A. QC material

☐ QC material deterioration
☐ Insufficient
☐ Bubbles/clots in material
☐ Preparation of material
☐ Wrong QC material
☐ Others material problems. Specify:……

B. ANALYSER

☐ Photometer problems
☐ Pipetting /probe system problems
☐ Other analyser hardware problems. Specify:…….

☐ Analyser software problems. Specify:…….

C. REAGENTS

☐ Reagent deterioration
☐ Other reagent problems: Specify:…….

D. CALIBRATION

☐ Calibration expired
☐ Wrong calibrator value inserted
☐ Other calibration problems: Specify:……

E. OTHER

☐ Unidentified
☐ Other causes: Specify:……

10. PROBLEMS RESOLUTION

☐ Immediately solved (< 3 hours)
☐ Analyser repaired by engineer; Resolved date & time:…….
☐ Call application specialist. Resolved date & time:……
☐ Stop analysis (all systems). Resolved date& time:……
☐ Revise procedure:……
☐ Change method: ……..

Appendix 5

List of EQA providers for every participating analytes

No	EQA PROVIDER	ANALYTES
1	**RCPA**	
	AMMONIA	Ammonia
	NEONTAL BILIRUBIN	Total Bilirubin
		Conjugated Bilirubin
	BLOOD GAS	pH
		pCO2
		PO2
	CSF	Total Protein
		Glucose
	Condensed Chemistry	Albumin
		AST
		ALP

ALT

Amylase

Total Bilirubin

Conjugated Bilirubin

Calcium

Chloride

Cholesterol

Cholinesterase

Creatine Kinase

Creatinine

Ferritin

GGT

Glucose

HDL

Iron

TIBC

Lactate

LDH

Magnesium

Osmolality

Phosphate

Pottasium

Protein

	Sodium
	TG
	Troponin T
	Urate
	Urea
	Cortisol
	BHCG
	FT4
	TSH
RCPA Immunoglobulin :Thyroid Antibodies	Anti TG
	Anti TPO
RCPA Urine Microscopy	Urine Biochemistry and Microscopy

2 RIQAS IMMUNOASSAY

	AFP
	CA 125
	CEA
	CORTISOL
	FERRITIN
	FOLATE

FT3

FT4

FSH

BHCG

LH

ESTRADIOL

PROGESTERONE

PROLACTIN

TPSA

TESTOSTERONE

TSH

VITAMIN B12

THYROGLOBULIN

iPTH

3 URINE RIQAS

Urine Amylase

Urine Calcium

Urine Chloride

Urine Creatinine

Urine Glucose

Urine Magnesium

Urine Microalbumin

Urine Phosphorus

Urine Pottasium

Urine Total Protein

Urine Sodium

Urine Urea

Urine Uric Acid

Urine Osmolality

4 Specific Protein

C-Reactive Protein

RF

Complement, C3

Complement, C4

IGA

IGG

IGM