Challenges For Quality Achievement In Clinical Biochemistry Reporting

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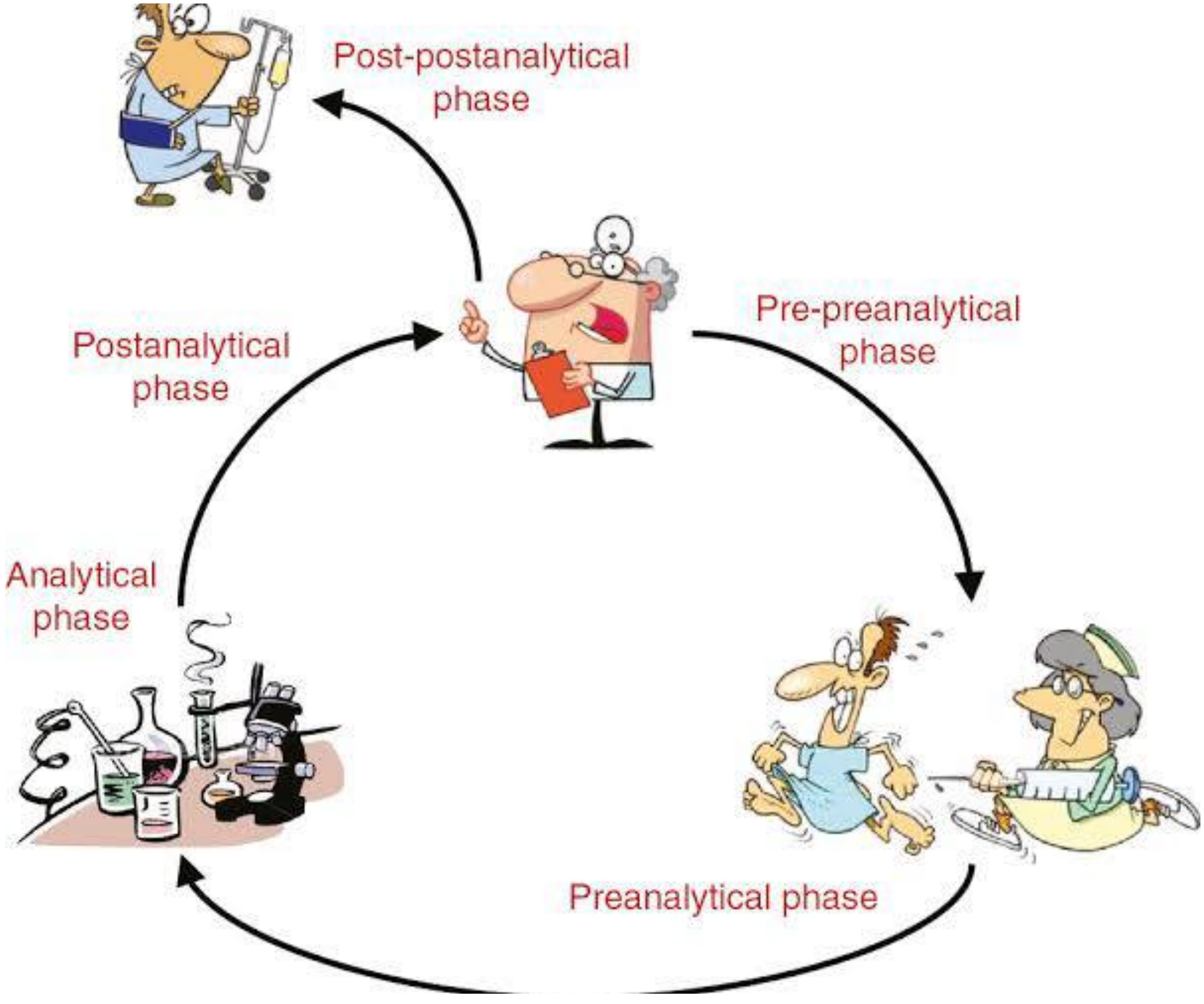

Post-postanalytical phase
Pre-preanalytical phase
Preanalytical phase
Analytical phase
Postanalytical phase

The Error - According to Work Zone

Pre-analytical Error

Analytical Error

Post-analytical Error

Pre - Analytical Error

Pre-Analytical Error

Most critical Phase

Chances of Error

In

Pre-Analytical Error = Approx. 50 - 70 %

Analytic error = 10 - 15 %

Post Analytical Error = 20 - 30 %

Process of The Pre-Analytical Area

1. **Patient Preparation**
2. **Sample Registration**
3. **Sample Request**
4. **Sample Collection**
5. **Sample Transport**
6. **Sample Shorting - Accession**
7. **Environmental Condition**

Pre-Analytical Error

◉ Error in Patient Preparation

✓ Fasting is require in

- Glucose Tolerance Test (GTT)
- Lipid Profile -
  - **Is only cholesterol estimation require fasting sample????**

✓ With Specific Cardiac Markers -

- Sample Collection at Specific Peak Hours

✓ Effect of Medicine

- Patient has not take Oral Hypo-Glycemic medicine before FBS,PP2BS
- Patient is on TPN (Total Parental Nutrition)

Pre-Analytical Error

◉ Error Sample Registration

- ✓ Wrong Entry - Manual Registration - Transcription Error
- ✓ LIS failure - Not Verified
- ✓ Entry Without ID / MRD
- ✓ No / Wrong Barcode / **Same Barcode for Different Vacuttee**

◉ Error Sample Request

- ✓ Mismatch ID with Request
- ✓ Un-identifiable Parameter - **Full LFT / Full RFT / All Enzyme**
- ✓ No / Inadequate patient's clinical history

Pre-Analytical Error

◉ Error in Sample Collection

✓ Wrong Collection Site

- ABG collection site - Venous sample
- Collection from Infusion Site -
  - Total Parental Nutrition - RL infusion
- FNAC from Wrong site

✓ Wrong Collection Time

- FSH / LH / GTT / Lipid Profile
- FBS , PP2BS

Pre-Analytical Error

- **Error in Sample Collection**
  - **Wrong Vacuette**
    - Routine Biochemistry in EDTA
      - Dis-arrange Electrolyte - High Potassium , Low Calcium
      - **Which biochemistry test is possible from EDTA?**
  - **Wrong Preservative Ratio**
    - ABG - Clotted Sample - Wrong Interpretation
    - APTT/PT - Wrong interpretation

Pre-Analytical Error

◉ Error in Sample Collection

✓ Wrong Method of Collection

- Haemolytic of The Blood Sample

✓ Small Needle

✓ Spirit wet area

✓ Forceful - Aspiration & Emptying of syringe in vacutte

✓ Tight tourniquet - Collection with Unreleased tourniquet

★ High Potassium

★ High Enzymes

★ Low Cell Count

★ **What about Sodium & Glucose ?**

Pre-Analytical Error

◉ Sample Transportation

- ✓ Haemolysis due to High temperature & Shaking
- ✓ Long Distance - Increase TAT
- ✓ Slide / Vacuttee - Not Secure
- ✓ Cross contamination
- ✓ Accident - Loss of Sample Bag

Pre-Analytical Error

◉ Sample Centrifugation - Accession

✓ High Speed & More Time

- Haemolysis
- Leakage
- Contamination

✓ Low Speed & Less Time

- Incomplete separation

✓ Imbalance

- Accident - Incident - Spillage - Breakage

Pre-Analytical Error

◉ Sample Shorting

✓ No Secondary Sample Identification

✓ Carry Over - Sample Separation - Same Micropipette Tips

✓ Re - Utilisation of Aliquot

- Contamination with Glycerol - Hypochloride
  - High Glucose
  - High Uric acid
  - High Cholesterol
  - POD Reaction

Pre-Analytical Error

◉ Environmental Condition

✓ Privacy

- Patient does not reveal the history

✓ No availability of Comfortable Chair

- Syncope - Incomplete collection

Pre-Analytical Error

Most Common Area

- Wrong or Missing **Identification**
- **Haemolysed**, clotted, and insufficient samples
- Inappropriate **Containers**
- Inappropriate blood to **Anticoagulant Ratio**
- **Missing** sample and/or Test request
- **Contamination** from infusion route
- Inappropriate **Transport and Storage** conditions.

Day to Day Pre - Analytical Issue Impact On Analyte Result

Important of Drug & Medical History

- **pO2 - 300 mmHg ————?????**
- **Plasma Glucose Report - Highly Lipemic————————?????**
- **TSH - 0.0006 IU/L With Normal T3 &T4 ———————— ??????**

Pre- requisite of Patient & Collection

- **ABG Sample - Sodium 180 mmol/L ———————— ???????**
- **K/C/O Diabetic ———— ??????**
  - **FBS - 100 mg%**
  - **PP2BS - 300 mg%**
  - **HbA1c - 6.0 %**

Day to Day Pre - Analytical Issue Impact On Analyte Result

Important of Drug & Medical History

- **pO2 - 300 mmHg ——— Ventilation With High FiO2**
- **Plasma Glucose Report - Highly Lipemic———— Uncontrolled DM**
- **TSH - 0.0006 IU/L With Normal T3 &T4 ——— Long Term Thyroxin**

Pre- requisite of Patient & Collection

- **ABG Sample - Sodium 180 mmol/L —— Sodium Heparin as Anticoagulant**
- **K/C/O Diabetic ——— Patient forgot to take drug at time of food**
  - **FBS - 100 mg%**
  - **PP2BS - 300 mg%**
  - **HbA1c - 6.0 %**

Analytical Error

Analytical Error

- Due to **Wrong Specification** of Instrument / Method
- Due to **violation in Performance** specification
- Due to **Quality Control**
- Due to **Calibration**
- Due to **Clinical Condition** of The Patient

Analytical Error

Drafting Specification for Equipment

- **According to Analyte / Laboratory Size / Work Load / TAT**
  - Semi — Fully Auto Analyser
  - Wet Chemistry — Dry Chemistry
  - ELISA — CLIA — ELFA

Drafting Specification for Reagent

- Liquid stable / Lypholized reagent
- Ready to use / Require to mix
- Pack size - Small / Big
- Method - Principle
  - **Urine Protein** - Sulphosalicylic Acid / Pyrogellol Red
  - **ALT** - With / Without PLP

Cholinesterase Kit Literature

2 Thiocholine + 2 [F

SPECIMEN C

Serum or heparinised or EDTA plasma is suitable. Serum or plasma samples remain stable for 14 days at 2-8^{0}C.

KIT PRESENTATION:

PACK SIZE	1 X 20 ml	1 X 40 ml	2 X 50 ml
R1- Cholinesterase (Buffer)	1 X 16 ml	1 X 32 ml	2 X 40 ml
R2- Cholinesterase (Substrate)	1 X 04 ml	1 X 08 ml	2 X 10 ml

WORKING REAGENT PREPARATION

Mixing 4 volumes of R1-Cholinesterase (Buffer) with 1 volume of R2- Cholinesterase (Substrate). i.e. 800 µl R1 + 200 µl R2.

REAGENT STORAGE AND STABILITY

All reagents are stable at 2-8^{0}C until the expiry date stated on the label. Do not freeze the reagents and **protect form light.**

NORMAL VALUES:

- Female : 3930 – 10800 IU/L
- Male : 4620 – 11500 IU/L

Each laboratory should establish its own reference range.

SENSITIVITY / LIMIT OF DETECTION:

The lower limit of detection is 55 U/L

CALCULATION:

Cholinesterase Activity (IU/L) = ΔA/min X 55000

LINEARITY:

This method is linear up to **20,000 IU/L**. For values above 20,000 IU/L, dilute the sample suitably with 0.9 % saline, and repeat the assay. Apply correction due to dilution to arrive at a final result.

REFERENCES:

1. Recommendation of the German Society for Clinical Chemistry. Standardization of methods for the estimation of enzyme activities In biological fluids: Standard method for the determination of Cholinesterase activity. J Clin Chem Clin Biochem 1992;30:163-70.

2. Thomas L, Clinical laboratory diagnostics, 1st ed frankfurt: TH-Books Verlagsgesellschaft; 1998. P.65-71.

3. Hallbach J, Klinische Chemie fur den Einstieg. 1st ed Stuttgart: Thieme;2001. p.143-4.

IFU No.: 010/00 | Rev. No.: 00/120723

Expiry Date | IVD In-Vitro Diagnostics Use | Storage | Mfg. Date | LOT Batch Number | REF Catalogue Number | See Package Insert

PATHOZYME DIAGNOSTICS
An ISO 9001:2015, ISO 13485:2016, CE & GMP Certified Company
A-115, Kagal Five Star MIDC, Kagal, Dist. Kolhapur-416 216.
Tel: 0231-2305072, Cell: +91 [illegible] 67810, E-mail: contactus@pathozyme.com, Website: www.pathozyme.com

Cholinesterase should have Lower limit of Detection 100 IU/L

Performance Check Done - LOD - 1000 IU / L

Analytical Error - Limitation of Performance

Performance Specification Required

- Accuracy , Precision ,Linearity
- Limit of Blank (LOB)
- Limit of Detection (LOD)
- Measuring Interval

For Better Understanding of Performance

Blood Urea - 300 mg % (GLDH Method) -

Potassium - 9.0 mmol/L (ISE Method) -

Serum Protein - 0.5 gm% (Biuret Method) -

S. Creatinine - 8.0 mg% >>>**Repeat Analysis - 8.6 mg% -**

RMSDI = (- 1.5%) >>>**RMDev% = (-7%)** >>>

Analytical Error - Limitation of Performance

Performance Specification Required

- Accuracy , Precision ,Linearity
- Limit of Blank (LOB)
- Limit of Detection (LOD)
- Measuring Interval

For Better Understanding of Performance

Blood Urea - 300 mg % (GLDH Method) - *Check Linearity*

Potassium - 9.0 mmol/L (ISE Method) - *Check Reportable Range*

Serum Protein - 0.5 gm% (Biuret Method) - *Check LOD*

S. Creatinine - 8.0 mg% >>>Repeat Analysis - 8.6 mg% - *Check Precision*

RMSDI = (- 1.5%) >>>RMDev% = (-7%) >>> *Check Accuracy*

Analytical Error - Due to Clinical Condition

- **Chronic Alcoholic - Chronic Liver Disease - Malnutrition**
  - **B6 Deficiency** - ALT, AST estimation ??
  - **Jaundice** - Very High Bilirubin - **Interference ????**
- **Uncontrolled DM** —- What can be very high ???
  - ELISA method affected
  - All most all biochemistry affected
- **Haemoglobinopathy** - HbA1c error

Analytical Error - Due to Methodology

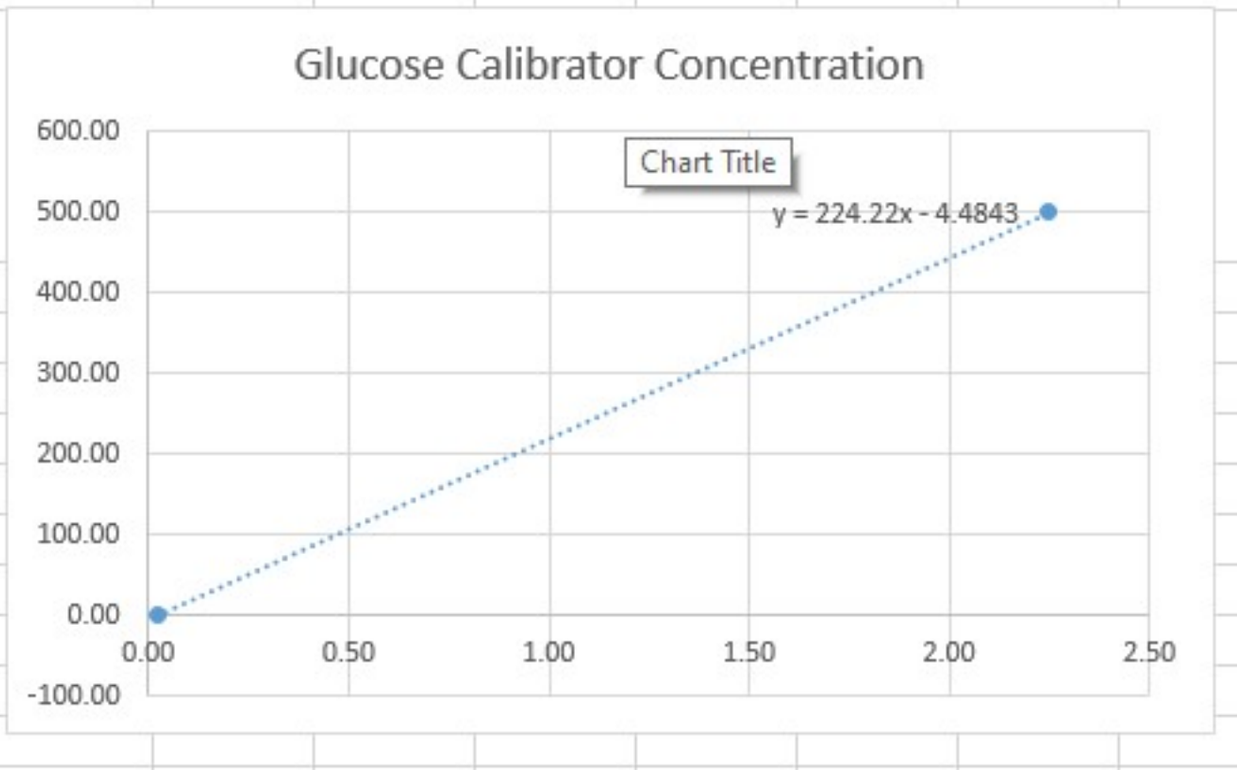
- **If Laboratory has made any change in**
  - **Analyte methodology ,**
  - **Sample / Reagent Volume,**
  - **Incubation time,**

◉ What get affected ???

◉ What to do ???

Analyte Error - Due to Calibration

O.D.	Glucose Calibrator Concentration
0.02	0.00
2.25	500.00



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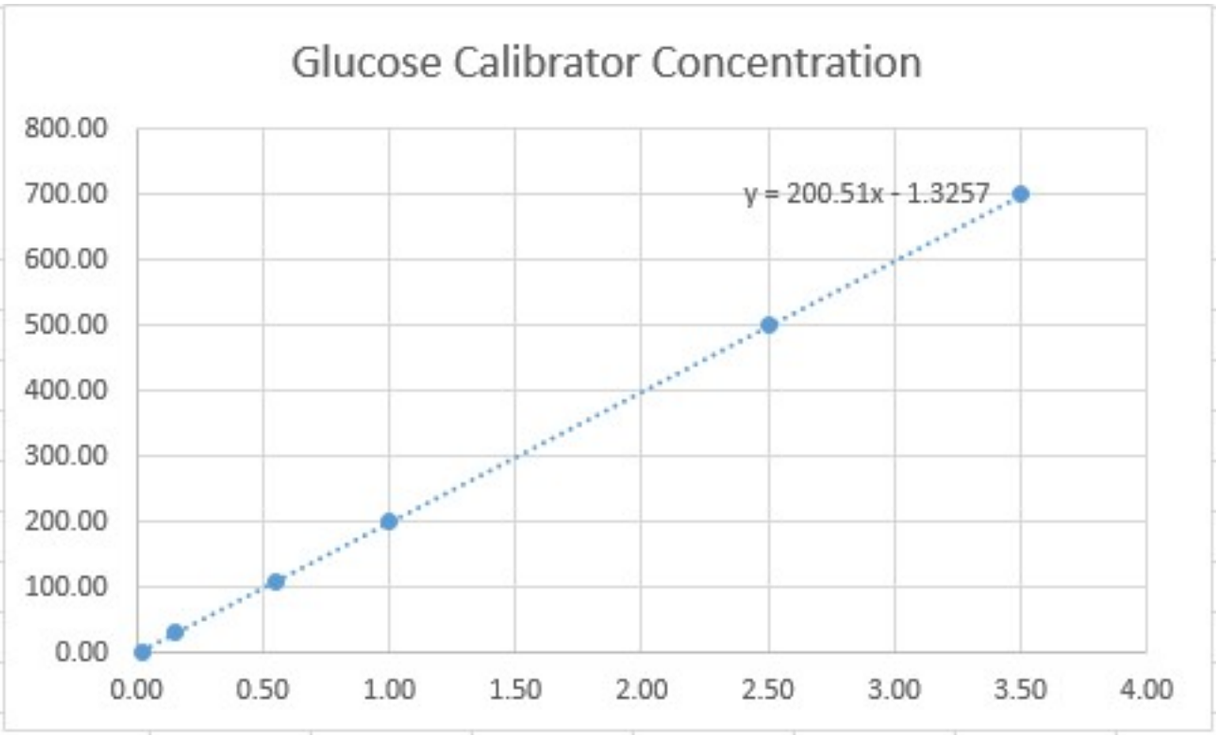
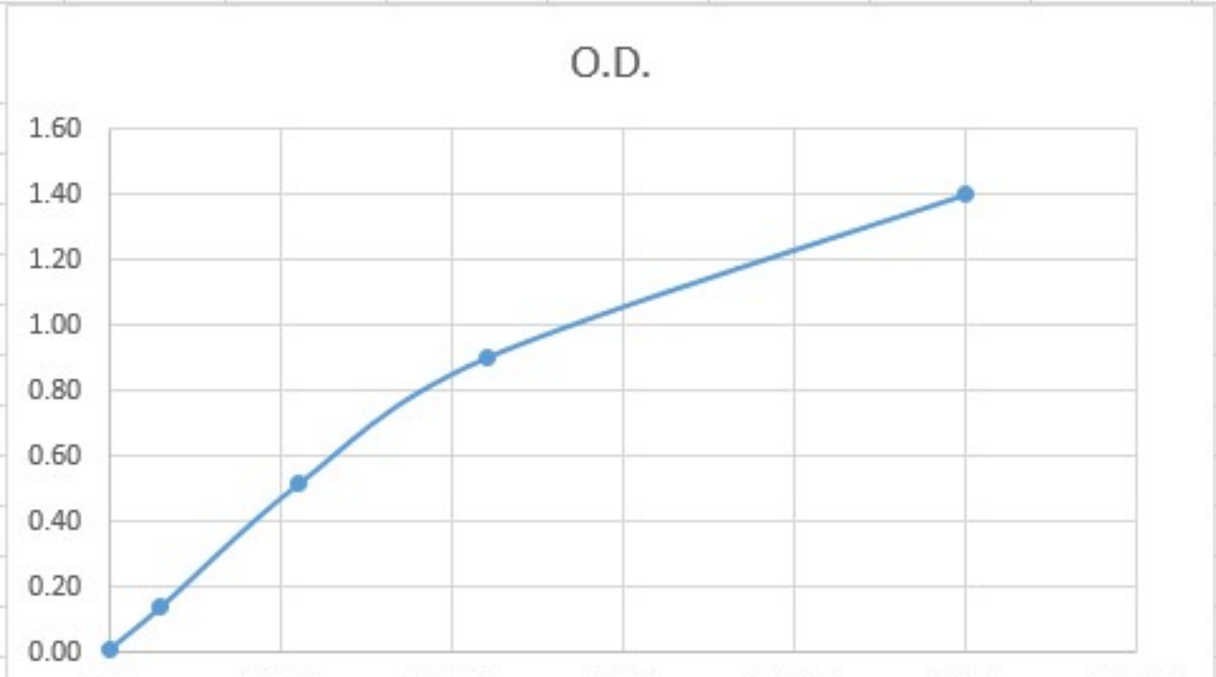
O.D.	Glucose Calibrator Concentration
0.02	0.00
0.15	30.00
0.55	110.00
1.00	200.00
2.50	500.00
3.50	700.00

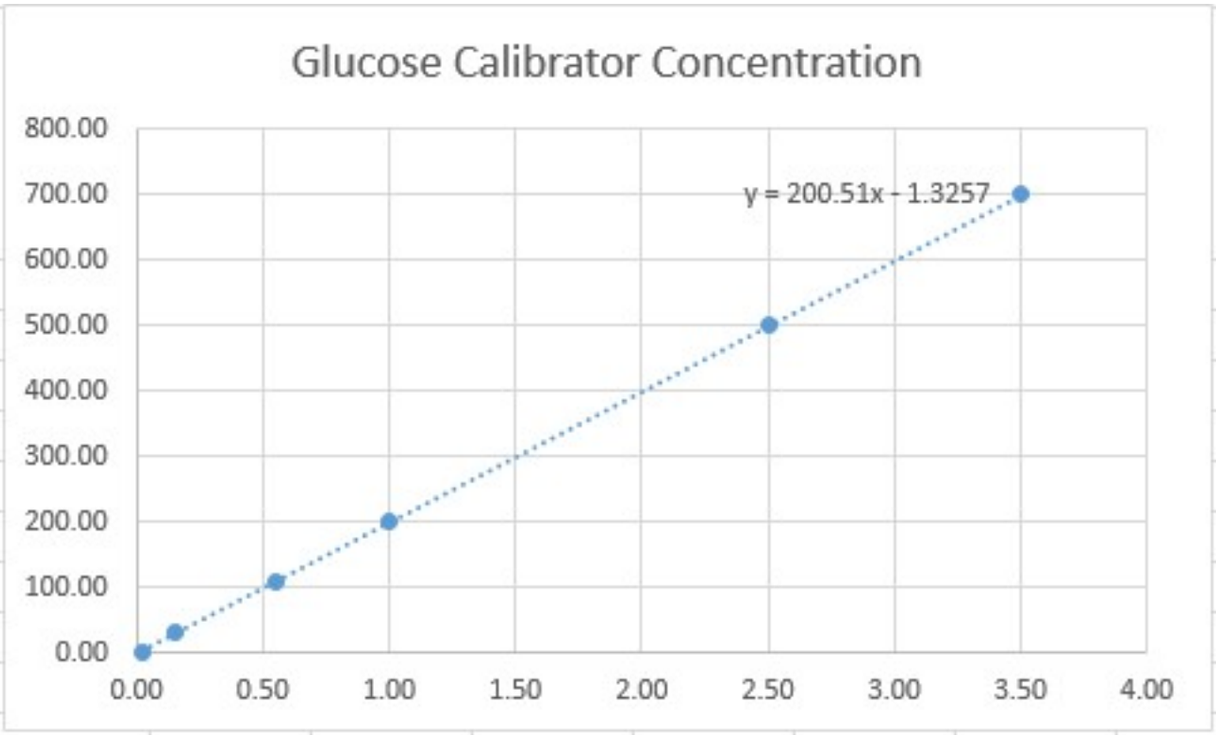


Analyte Error - Due to Calibration

Glucose Calibrator Concentration	O.D.
0.00	0.01
30.00	0.14
110.00	0.51
220.00	0.90
500.00	1.40



O.D.	Glucose Calibrator Concentration
0.02	0.00
0.15	30.00
0.55	110.00
1.00	200.00
2.50	500.00
3.50	700.00



Calibration of Analyse should be

- 1st Point - Lower range
- 2nd Point - Reference range
- 3rd Point - Clinical decision range
- 4th Point - Higher range

Analytical Error - Due to QC

Quality Control Validation - IQC , EQAS , Comparability

Internal Quality Control

- Inadequate Frequency
- Irrelevant Timing of IQC run
- Wrong selection of Level of IQC
- Wrong L-J Chart = High SD
- No RCA for IQC Outlier
- No IQC Trend / Shift Analysis

External Quality Assurance Scheme

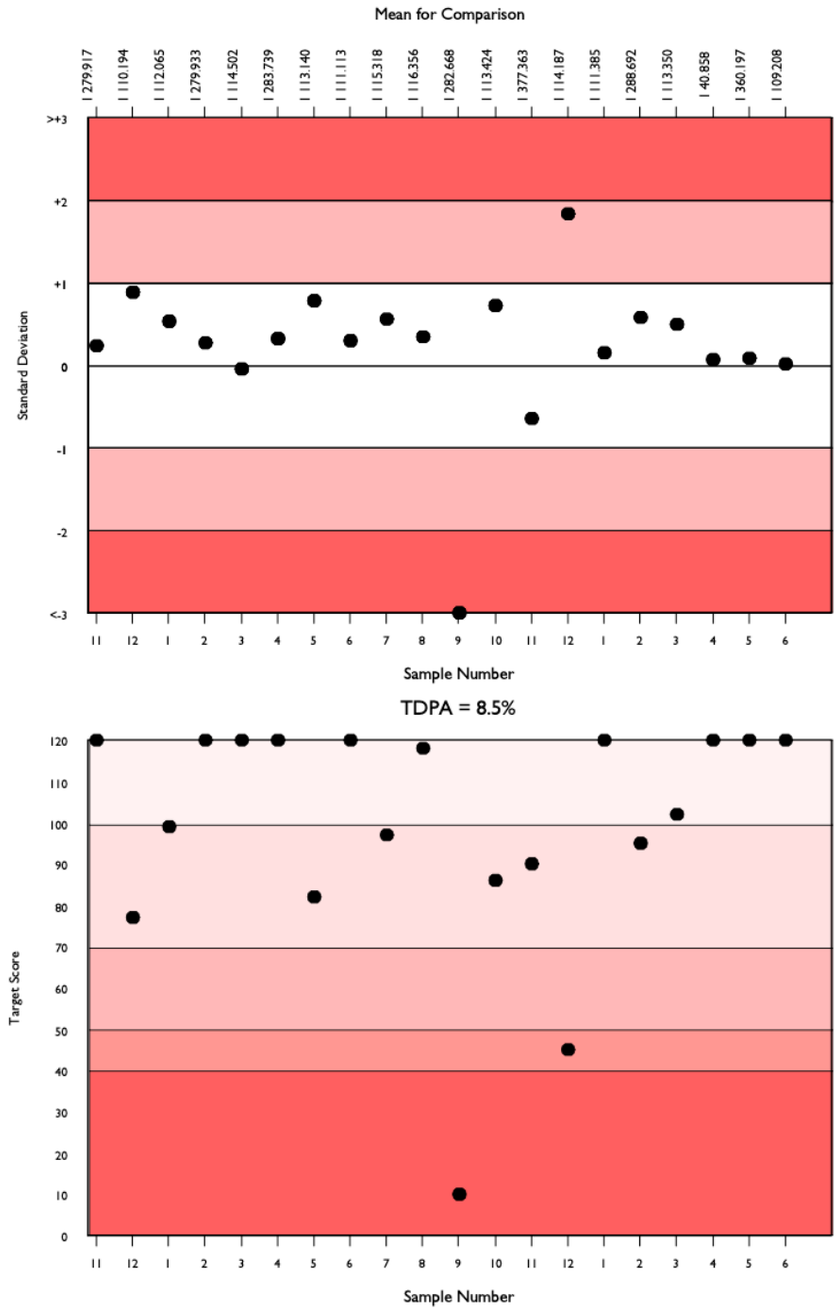
- Mostly observe SDI & Dev%
- **But RMSDI & RMDev% - ?????**

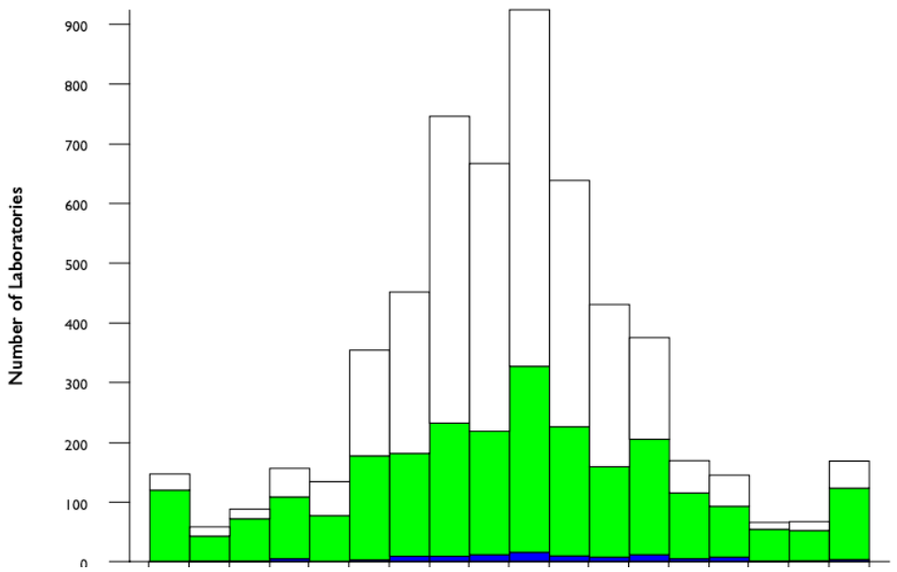
Glucose, mg/dl

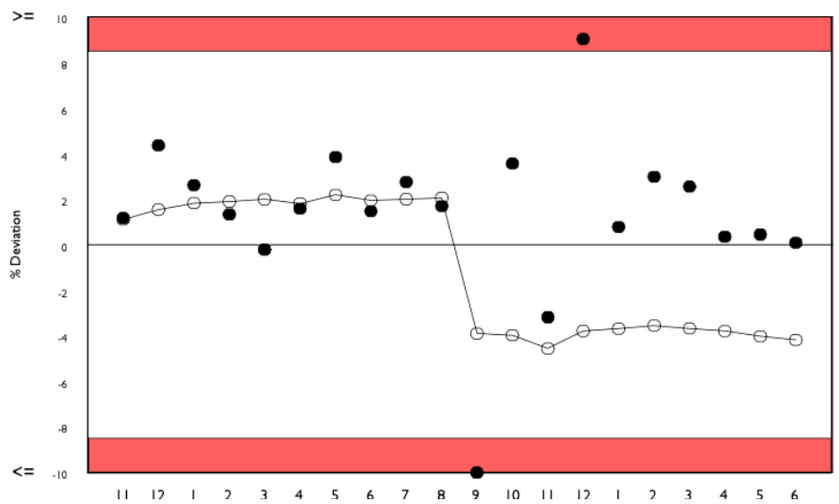
	N	Mean	CV%	U_m	SDPA	Exc.
All Methods	5320	107.817	3.9	0.07	5.57	463
Glucose oxidase	2399	107.898	5.3	0.14	5.58	185
Erba XL Series	98	109.208	4.0	0.55	5.64	8

▲ Your Result	109.300	SDI	0.02
		RMSDI	-0.86
Mean for Comparison	109.208	TS	120
		RMTS	90
		%DEV	0.1
		RM%DEV	-4.2

Acceptable limits derived from Biological Variation	6.96%
Acceptable limits of performance for RIQAS	8.50%







LD (LDH), U/l @ 37°C

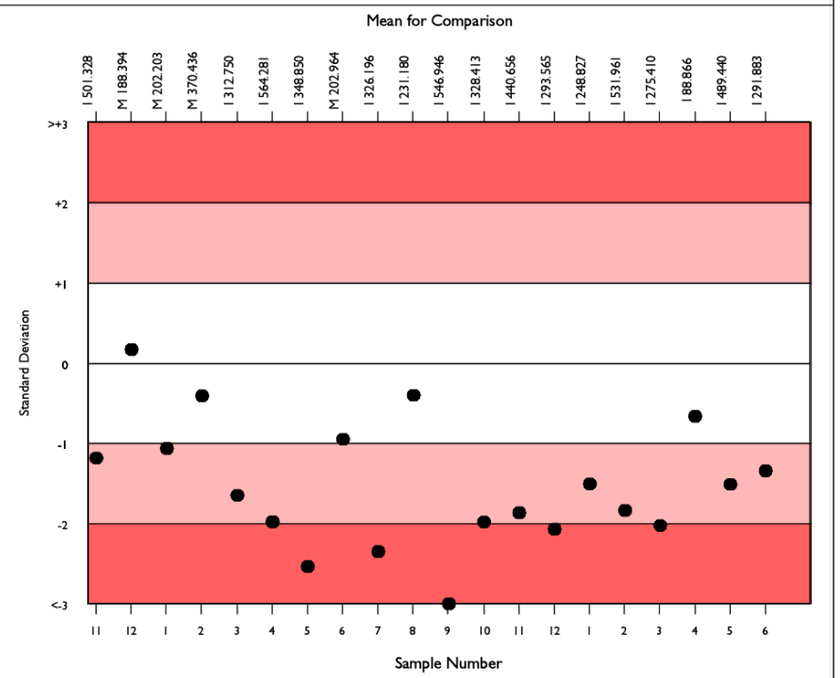
	N	Mean	CV%	U_m	SDPA	Exc.
All Methods	2482	221.031	31.8	1.76	17.60	170
L to P, IFCC	1430	185.344	4.4	0.27	14.76	136
Erba XL Series	6	291.883	43.9	65.43	69.44a	0

▲ Your Result	198.500	SDI	-1.34
		RMSDI	-1.80
Mean for Comparison	291.883	TS	11
		RMTS	12
		%DEV	-32.0
		RM%DEV	-38.1

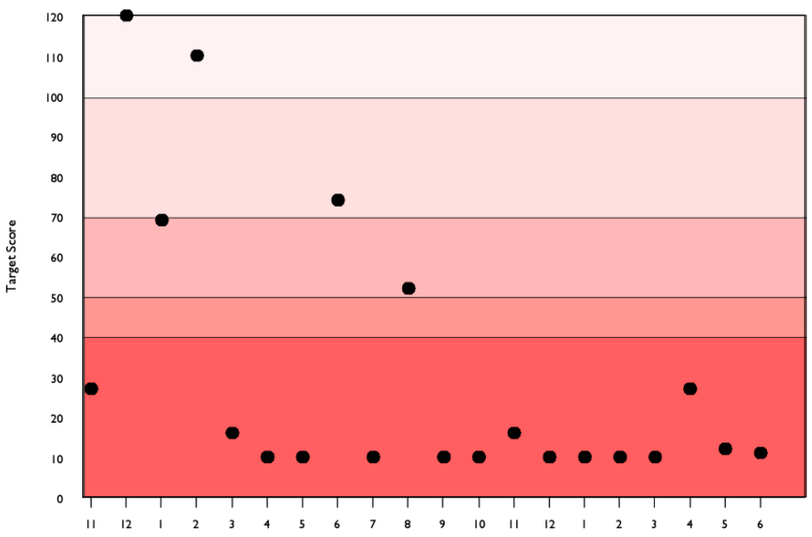
Acceptable limits derived from Biological Variation 11.4%

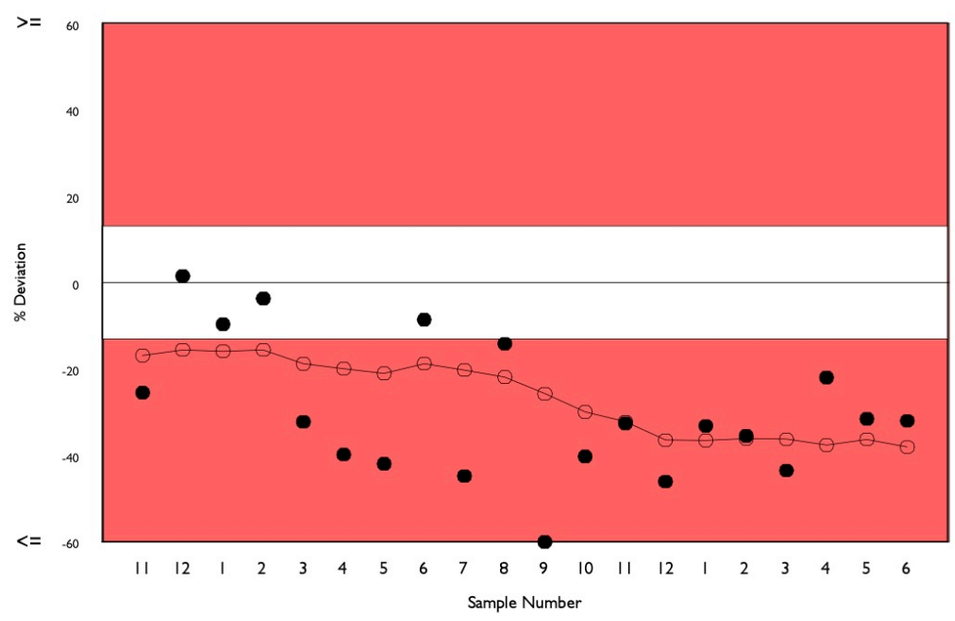
Acceptable limits of performance for RIQAS 13.10%

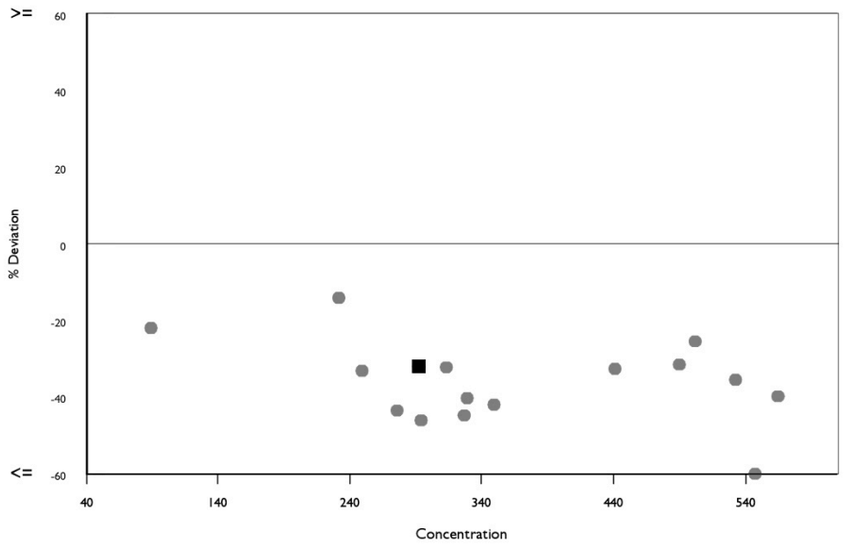
TS & %DEV outside limits



TDPA = 13.1%

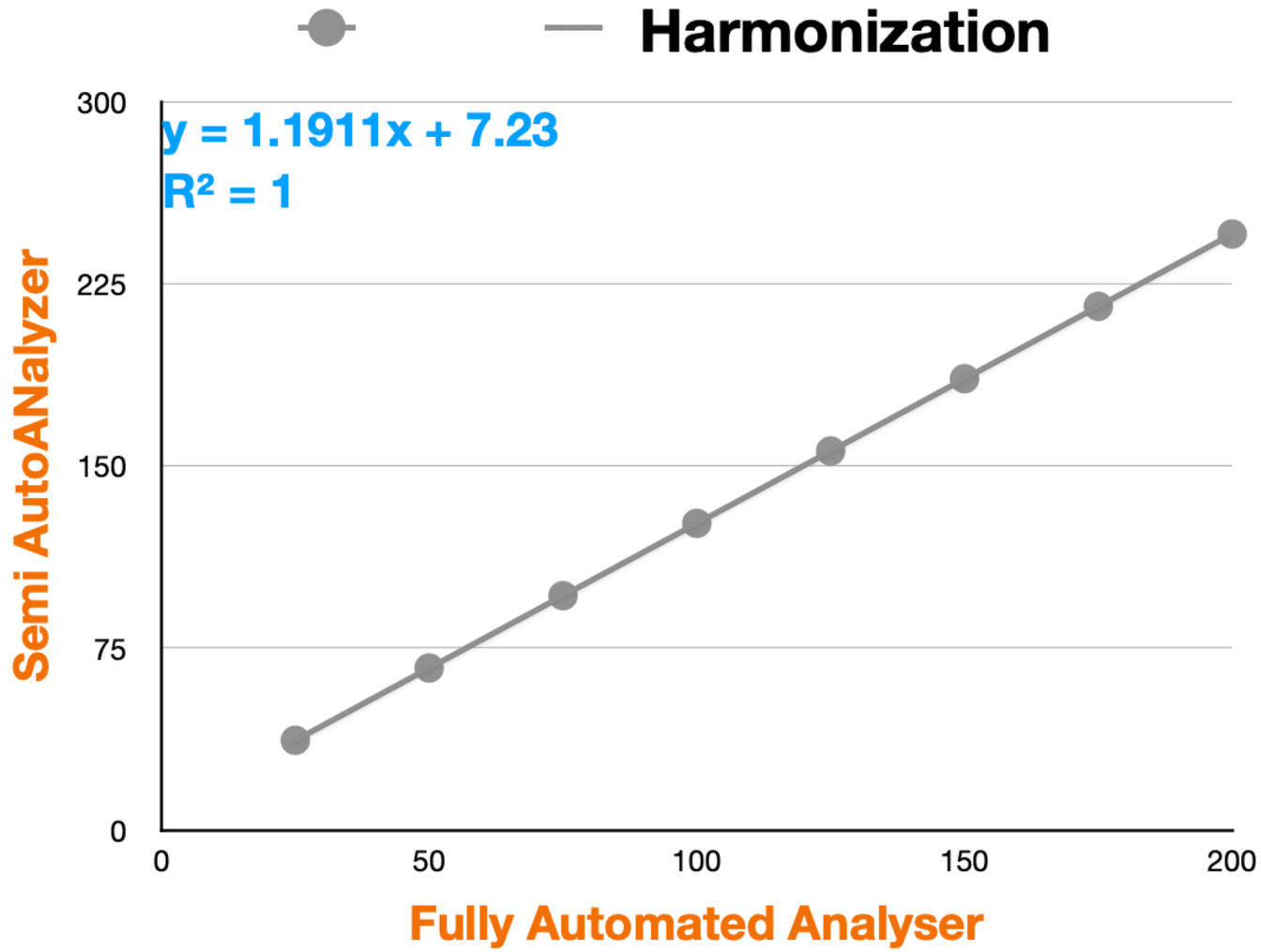






Analytical Error

- **Due to Inadequate Comparability - Harmonisation**
  - ✓ Use of Two Different Methods / Instrument



Post - Analytical Error

Post Analytical Error

Laboratory Information System

- Unverified / Non Validated LIS
- Error in Analyte LIS Interface Code
- No facility for Delta check

Report Format

- Biological Reference Range
  - Old Guideline / Non Scientific
  - Age / geographical Area
- Demographic Data mismatch

Transcription error - In case of Unidirectional Interfase

Critical informing

- No Cross Verification
- To wrong person or patient

TAT violation

Troubleshoot's For Quality Achievement In Clinical Laboratory

Way / Method
To Do
Troubleshoot's For Errors

1. Quality Indicator
2. Non Conformity Record
3. Root Cause Analysis
4. Risk Management - Preventive Management
5. Continual Improvement

Quality Indicator of Pre-Analytical Area

1. Number of samples collected in **inappropriate containers**
2. Number of samples **haemolysed** (haematology, chemistry)
3. Number of samples **clotted** (haematology)
4. Number of samples with **insufficient volumes**
5. Number of samples with inadequate **sample-anticoagulant ratio**
6. Number of **improperly labelled** samples
7. Number of **samples lost**/not received
8. Number of samples **damaged in transport**
9. Number of **improperly stored** samples

1st Way / Method Of Troubleshoot's

Quality Indicator of Analytical Area

1. Number of analyte's **TE% (total error)** violated TEa% (Total Allowable Error) as per guideline
2. Number of **Outlier** of analyte's IQC
3. Number of **EQAS /ILC score** violated satisfactory level.
4. Percentage of **mismatch result** in repeat analysis
5. Number of Reagent **lot verification** failure
6. **Downtime** of Analyser in month
7. Number / Percentage of **Calibration failure**

- Monitoring and evaluation of **CV %** of IQC
- **Trend** Analysis of L-J Chart
- Monitoring and Evaluation of Monthly **SDI score** of EQAS / ILC

Quality Indicator of Post-Analytical Area

1. Number or Percentage of Analyte violate **TAT**
2. Number or Percentage of report with T**ranscription Error**
3. **Number of patient's report not co-related with clinical history or previous result.**
4. Number of **critical report** are not informed
5. Number of critical informed report are **not cross verified**.

1st Way / Method Of Troubleshoot's

Implementation of Quality Indicator

➡Prioritised Quality Indicator

➡Define Bench Mark of Quality Indicator

➡Data Collection

➡Finding Outliers

➡Root Cause Analysis

➡Corrective Action - Preventive Action - Risk Managment

➡Continual Improvement - Updation of Bench Marks

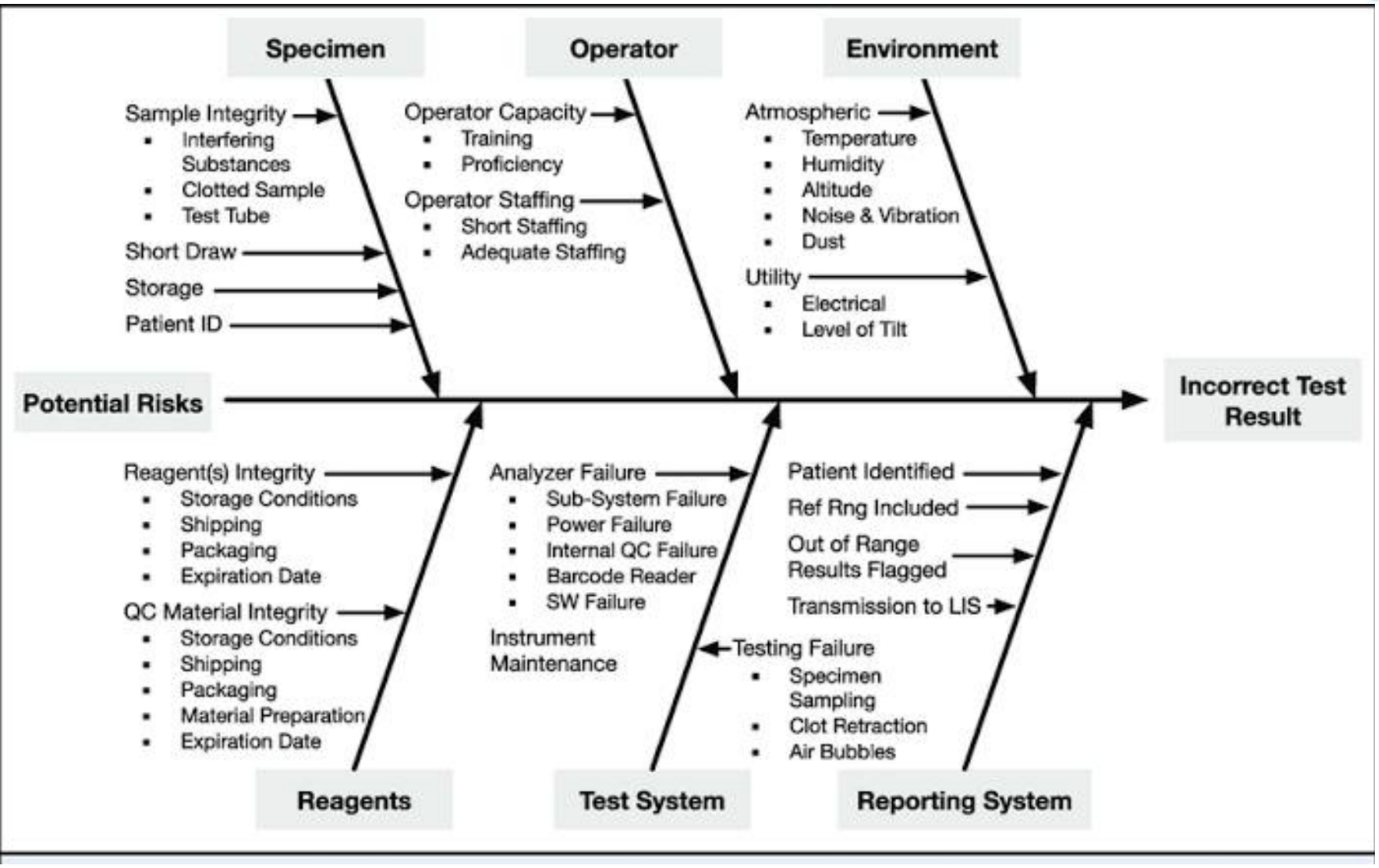
2nd Way / Method Of Troubleshoot's

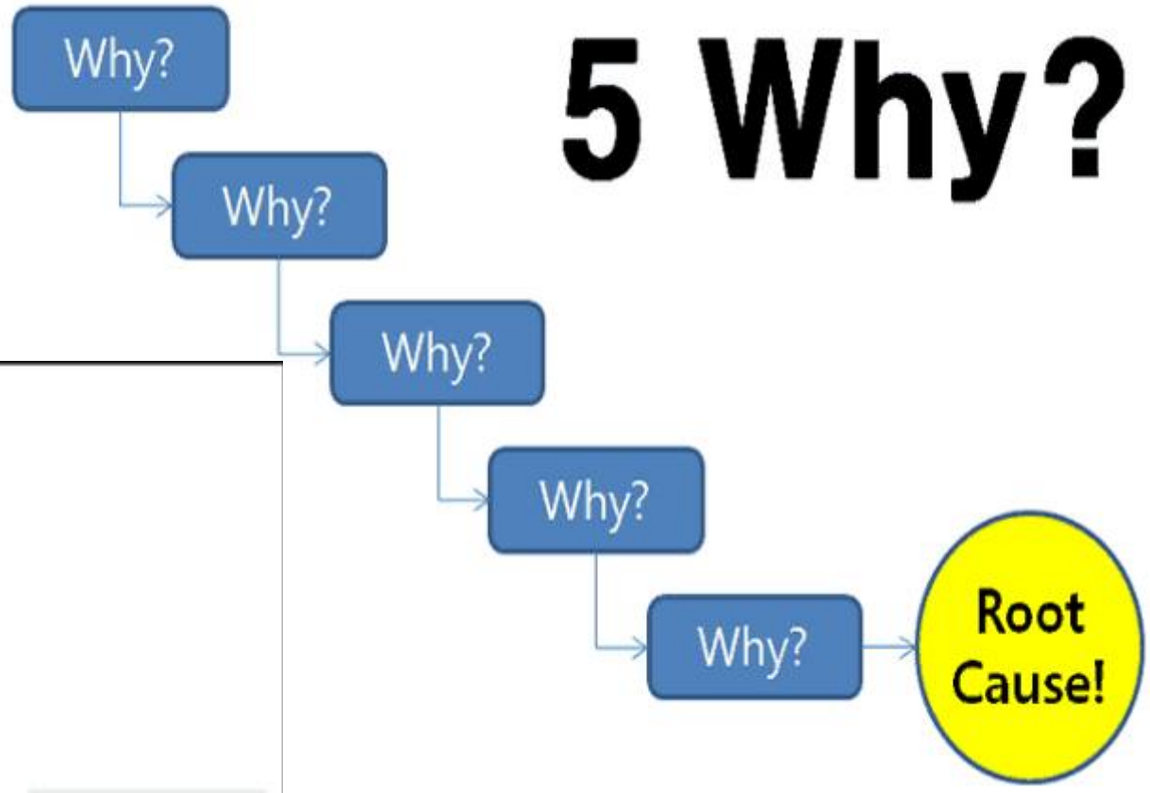
Non Conformity Records

1. Every **Violation of Quality Indicator** >>>>>>> Non-Conformity
2. Find and Do
   - **Immediate Action - Corrective Action**
3. **Root Cause Analysis**
   - Do accordingly **preventive action**
4. Document it - **Excel File - Easy to Short**
5. Monthly **short NC** - Find **Most Violated Part**
   - Most Commonly Violated **Personnel** / **Analyse** / **Instrument**
   - Most Commonly Violated **Clause** of ISO 15189
   - Most **Weak area** of Laboratory
5. **Risk Management**

3rd / Method Of Troubleshoot's

Root Cause Analysis





5 Why?

5' why technic

Ishikawa Technic - Fish Bone Technic

Risk Management

- Management of Possible Threat
- To minimise chance of Violation / Incident / Accident
- **Same as Preventive action**
- But It also **include** management of threat which is **not occurred before**.

5 Why Technic of Root Cause Analysis

More than 10% Sample Haemolysed
(Violation of Bench Mark)
in October 2023

5 Why Technic	Scenario - 1
1st Why	**New transport bag** was introduced and it unable to maintain temperature
2nd Why	Laboratory management has **not taken working demo** before purchase
3rd Why	**Vendor** for transport of bag was **well known**, old and faithful.
4th Why	Vendor **evaluation was not don**e with proper benchmark and it was just done on paper for NABL assessment.
5th Why	NABL accreditation process was implemented in laboratory from **consultant** - **(Root Cause)**
Corrective Action	Management asked Vendor to **correct transport bag** immediately for temperature maintaining facility.
Preventive Action	Management asked his most competent and sincere laboratory person for "**4 Days Internal Auditor Training** as Per ISO 15189:2022 **&** set **priority for appointing** employee who has competency related ISO15189

5 Why Technic of Root Cause Analysis

More than 10% Sample Haemolysed
(Violation of Bench Mark)
in October 2023

5 Why Technic	Scenario - 2
1st Why	Most of sample collection is done by **untrained staff.**
2nd Why	Most of the sample are received from **referring hospital** and their nursing staff are not trained for sample collection and transportation.
3rd Why	Laboratory management has focused on **training of their own phlebotomist.** **(Root Cause)**
4th Why	————————
5th Why	————————
Corrective Action	Laboratory management asked their trained **phlebotomist** to remain at hospital at **peak hours of the hospital**.
Preventive Action	Laboratory management asked hospital management to give **chance /slot to train their nursing staff** for sample collection during any of their own training session.

5 Why Technic of Root Cause Analysis

More than 10% Sample Haemolysed
(Violation of Bench Mark)
in October 2023

5 Why Technic	Scenario - 3
1st Why	In Civil Hospital, Collected sample are brought by ward-boy **without cold chain**
2nd Why	Cold chain box are available but nursing staff does **not using it.**
3rd Why	Previously purchased cold chain box are **stolen.**
4th Why	Nursing incharge was **not** maintaining log-book for "**Cold Chain Box Log**"
5th Why	Nursing staff is **not sensitised to maintain** sample transportation log as well as sample transport bag log. **(Root Cause)**
Corrective Action	**Laboratory director** has **taken charge** and responsibility of all their "Cold Chain Box" and Started using it with maintaining it's traceability and log.
Preventive Action	**LD asked hospital admin to arrange sensitisation training about related Good Laboratory Practice for Nursing Staff. & asked Medical Superitendent to purchased GPS sensory for "Cold Chain Box", to track transport box, TAT and to evaluate activity of Ward-Boy.**

Result

Lost the kingdom

Therefore

Why

Lost the battle

Therefore

Why

One less warrior

Therefore

Why

One less horse

Therefore

Why

Horse lost a shoe

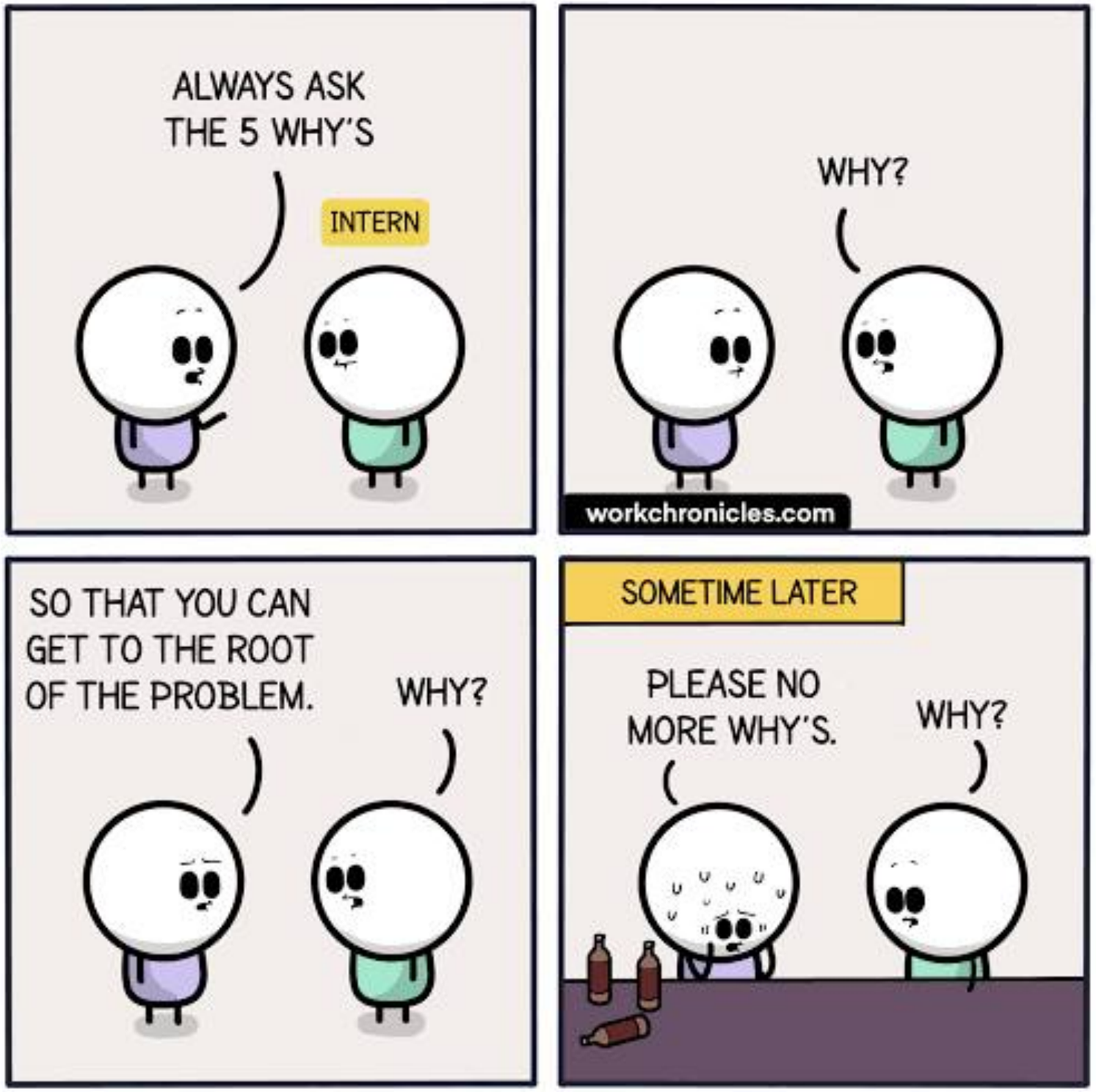
Therefore

Why

Not enough nails

Start

Root Cause



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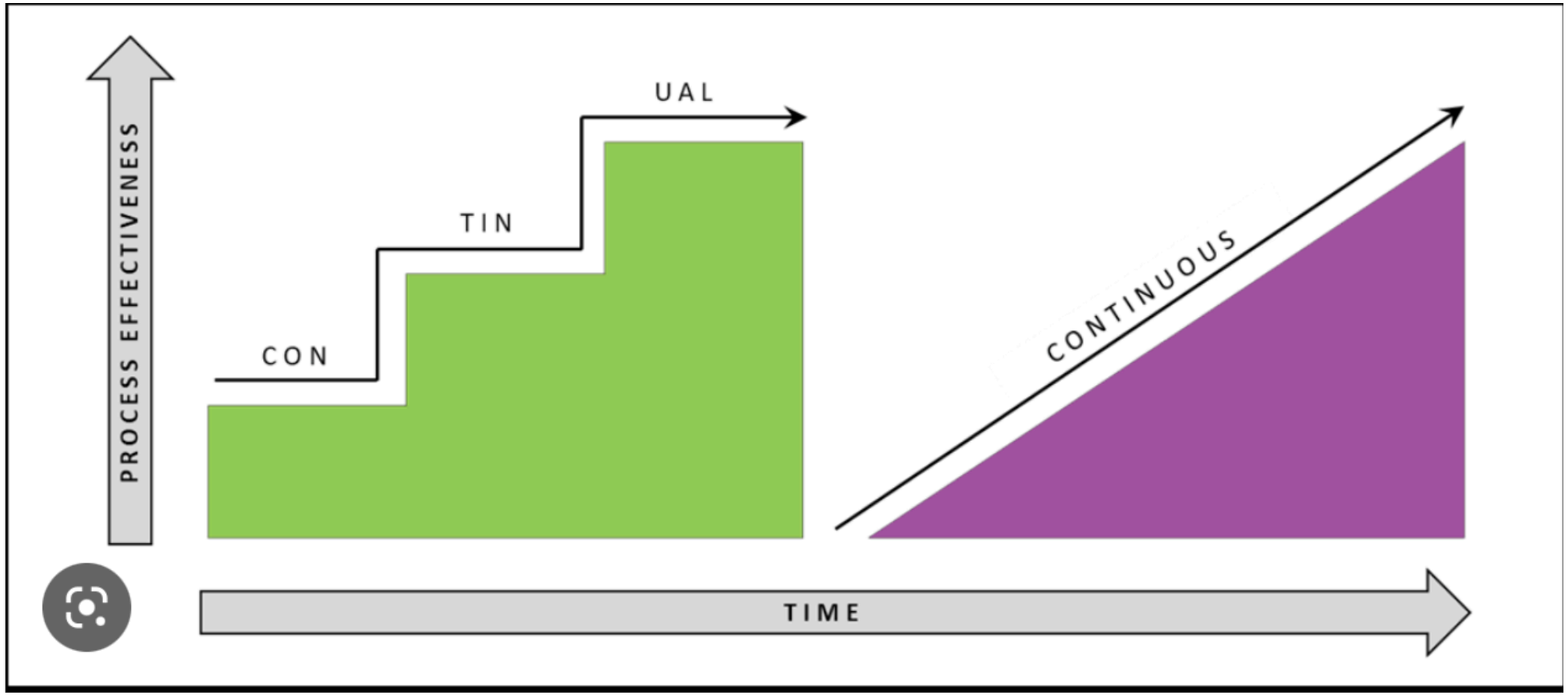
5th Way / Method Of Troubleshoot's

Continual Improvement



Continual

Do some Improvement

>>>

Sustain improvement

&

Move again for

Another level Improvement.

Continuous

Improvement will be

without break in process

Not possible

in medical laboratory

5th Way / Method Of Troubleshoot's

Continual Improvement

Process area Covered	Area of Improvement	Present Day Target	Target for 2024	Target for 2025
Examination	IQC Data Analysis	Monthly CV % < **50%** of TEa	Monthly CV % < **40%** of TEa	Monthly CV % < **30%** of TEa
Examination	EQA results	EQAS outlier in Less **10%** of parameter of the scope	EQAS outlier in Less **7%** of parameter of the scope	EQAS outlier in Less **5%** of parameter of the scope
Post - Examination	Overall objectives - TAT Analysis	TAT outlier < **10%**	TAT outlier < **5%**	TAT outlier < **3%**

Example For Continual Improvement

- XYZ large size laboratory
- Maintained Minimum Error >>>>> In Patient Registration.
- During Evaluation >>> **"User's Feedback"**
    1. Drinking facility is not available at reception.
    2. Patient waiting time at reception is high.
    3. Air-conditioning is not there at area around relative lounge.
- Laboratory selected 2nd point
    - Significant numbers of user's feedback of higher waiting time in registration area,
    - As per Highest Priority
- **This was never evaluated through defined Quality Indicator.**
- Made arrangement >>>> Addition Registration Counter >>> Improvement Activity.
- **Check effectiveness of the action take**
- **Added Quality indicator** for "**Monitoring of Waiting time at Registration Area**"

Thank You Very Much

Rajkot Association of Pathologist & Microbiologist

For

Inviting Me and Giving Chance To Connect With You

My Sincere,

Appreciation To You For Investing

Your Presence & Precious Time