# Automated Biochemistry Analyzer

# Issues and Troubleshooting

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# Clinical Chemistry Analyzer

There have been significant changes in clinical biochemistry over the last 30 years with the introduction of total laboratory automation.

Clinical chemistry analyzers run assays on clinical samples such as

- blood,
- serum,
- plasma,
- urine, and
- fluid

to detect the presence of analytes relating to disease or drugs.

Auto analyzers

- maximize throughput,
- improve user safety from biohazards, and
- diminish the risk of cross-contamination.

# Clinical Chemistry Analyzer

Analytes commonly include

- Enzymes ( AST :  Cardiac enzyme)
- Electrolytes ( Potassium : renal disorders),
- Specific proteins ( CRP : infections),  and
- Therapeutic drugs ( Methotrexate ).

The results give clinicians feedback on toxicology and on renal, cardiac, and liver function.

# Test methods used in autoanalyzers

Most common methods used are

- Photometry
  - End point : Glucose, creatinine, protein etc
  - Kinetic assay : AST, ALT, GGT etc
- Turbidimetry
- Ion selective electrodes
- EIA [ Enzyme immunoassay]
- CMIA [ Chemiluminescence Microparticle immunoassay ]
- Nephelometry

# Types of analysis

- Batch analysis is the ability to run a large number of samples in one run.
- Random and continuous access machines are more flexible for quick turnaround times.
- STAT machines have a sequence interrupt feature that gives precedence to urgent samples.

# Throughput

- Throughput is measured in tests per hour, but the rate varies depending on the test method.
- Because colorimetric tests have short incubation times, they are often quoted for high-throughput machines.
- The throughput rate for ISE is quoted separately.

# Data management on autoanalyzers

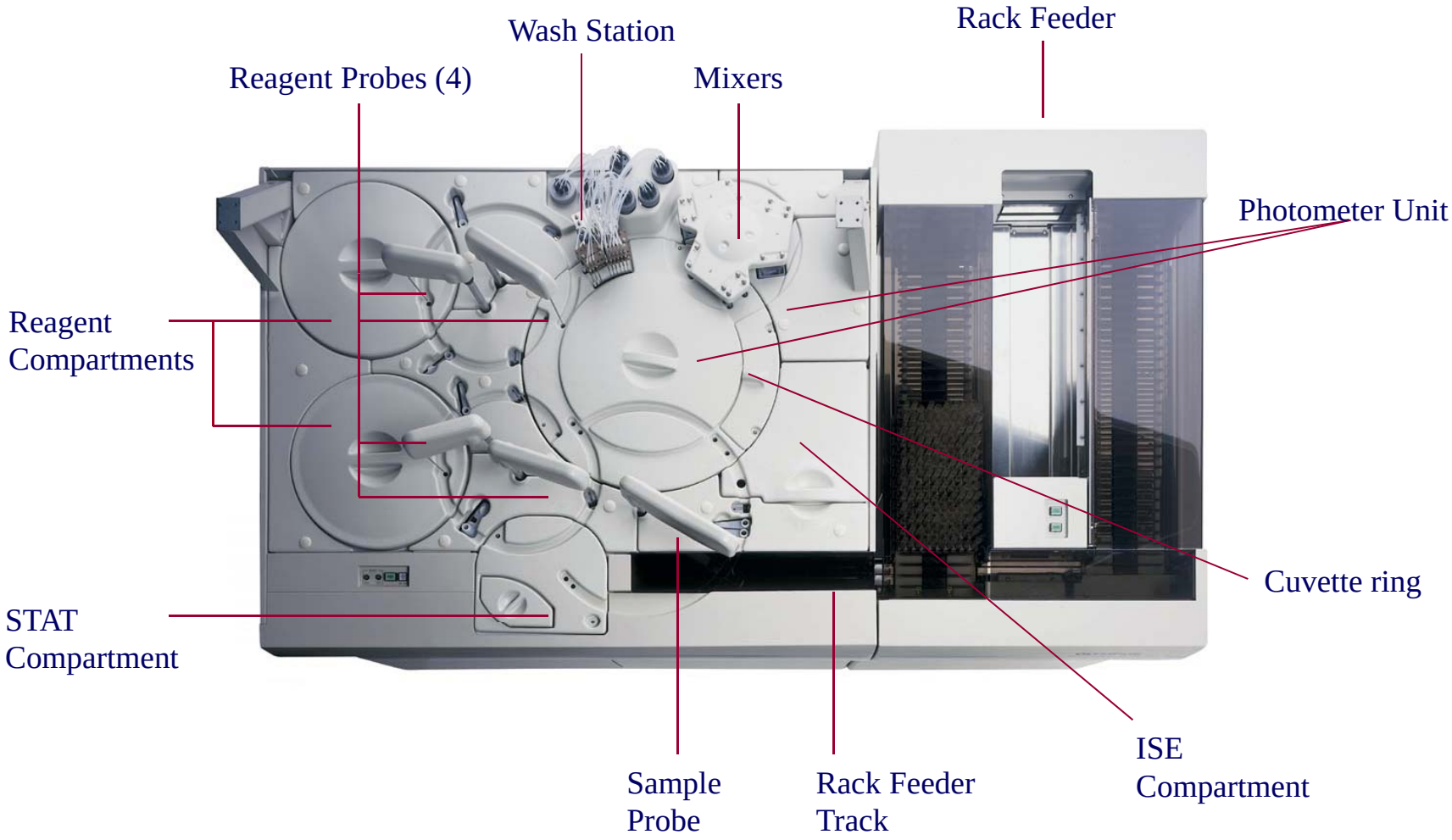
- For large laboratories where throughput can be hundreds to thousands of tests per hour, instruments include barcode handling and data management software.

- Often, analyzers can be linked to your existing LIS.

# Chemistry Analyzer Operation

| | | |
|---|---|---|
| IDENTIFICATION AND PREPARATION | | |
| 1. | Sample identification | This is usually done by reading the barcode.<br>This information can be entered manually. |
| 2. | Determine test(s) to perform | The LIS communicates to the analyzer which test(s) have been ordered. |
| CHEMICAL REACTION | | |
| 3. | Reagent systems and delivery | One or more reagents can be dispensed into the reaction cuvette. |
| 4. | Specimen measurement and delivery | A small aliquot of the sample is introduced into the reaction cuvette. |
| 5. | Chemical reaction phase | The sample and reagents are mixed and incubated. |
| DATA COLLECTION AND ANALYSIS | | |
| 6. | Measurement phase | Optical readings may be initiated before or after all reagents have been added. |
| 7. | Signal processing and data handling. | The analyte concentration is estimated from a calibration curve that is stored in the analyser. |
| 8. | Send results to LIS | The analyzer communicates results for the ordered tests to the LIS. |

# Aerial view of Olympus analyzer



# Why do laboratory errors occur?

# Why Analytical Results Vary

## Inter-individual Variation

- Age
- Sex
- Race
- Genetics
- Long term health status

## Intra-individual Variation

- Diet
- Exercise
- Drugs
- Sleep pattern
- Posture
- Time of venipucture
- Length of time tourniquet is applied

# Why Analytical Results Vary

## Pre-analytical Variation

- Transport
- Exposure to UV light
- Standing time before separation of cells
- Centrifugation time
- Storage conditions

## Analytical Variation

- Random errors
- Systematic errors

## Post-analytical

- Transcriptions errors
- Results reported to wrong patient

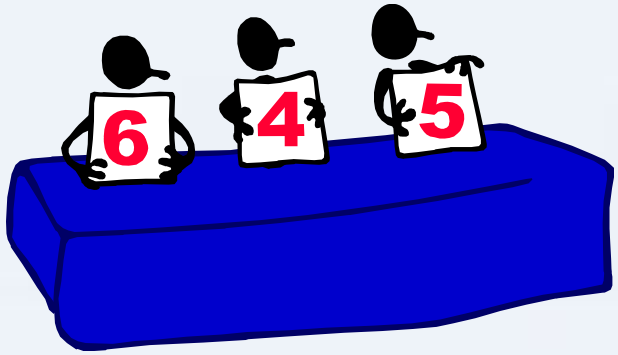
# How is the error observed?

- Systematic

*Avoidable error due to controllable variables in a measurement.*

Random

*Unavoidable errors that are always present in any measurement. Impossible to eliminate*




## Contamination or Carryover?

- Reagent probe / Mix Bar / Cuvette Contamination?
- Sample Probe Carryover?
- Laundry/ Improper washing

# Understanding the problem!!

- In order to troubleshoot a reported problem, the specific details must be clearly identified.

- Correct customer interpretation and clarity of analysis can help to minimise duration of investigation.

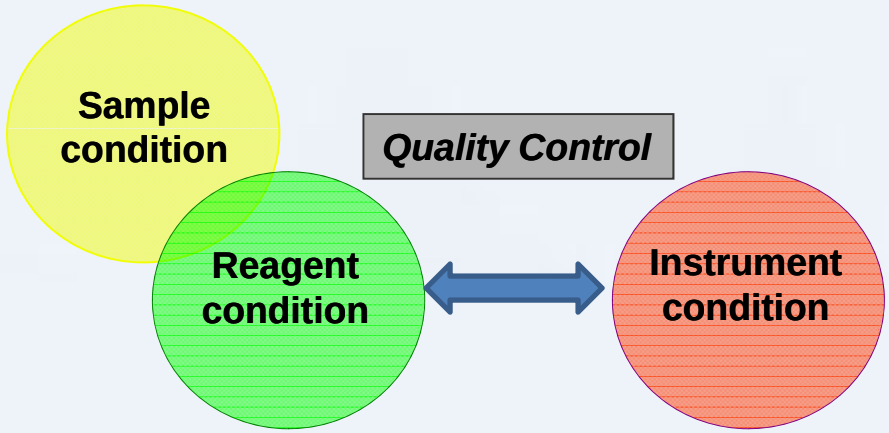
# Classification of problem

Problems can be divided into 3 main categories

1. Sample condition

2. Reagent condition

3. Instrument condition



# 1. Sample condition

Sample can be

a. Patient,

b. Calibrator or

c. Quality control

Kind of sample(serum,  plasma, urine, fluid)?

Fresh sample?

Cup or tube?

Sample change/alteration?

(concentration,evaporation,contamination)

# A. Patient sample condition

- Fibrin,
- Blood cells,
- Foreign objects,
- Lipemia,
- Icterus,
- Haemolysis
- Drug influence,
- Infusion (drip),
- Preservatives

# B. Quality control/calibration sample condition

- Dissolution,
- Mixing,
- Storage/temperature,
- Solution volume,
- Dissolution time,
- Preservation,
- Lot no.
- Target value,
- Method,
- Range

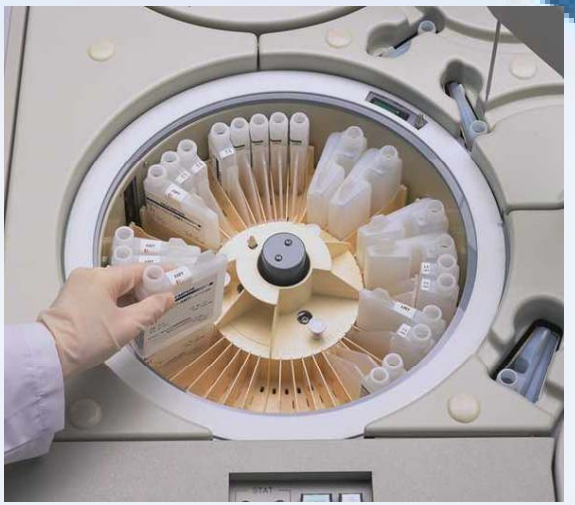
# EQAS ( External Quality Assurance Scheme)

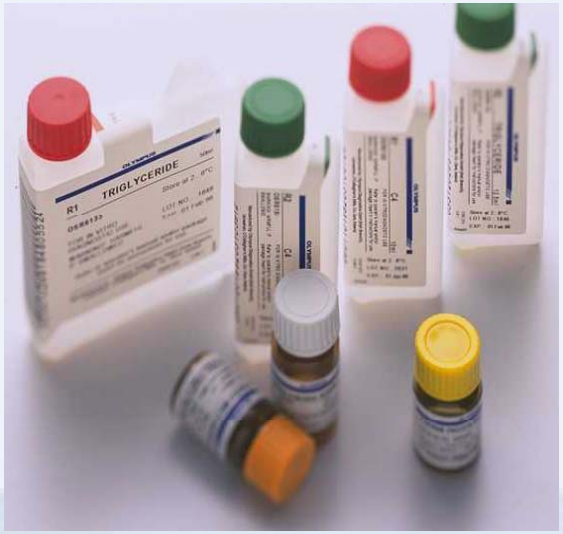
- EQA is also known as proficiency testing (PT).
- Blind samples submitted to laboratories.
- Labs must periodically analyze in order to assure quality for acceptable results.
- **Process the PT samples in the same run as patient samples**
- Accreditation Requirement – Mandatory Clause 5.6

# 2. Reagent Condition

Method or Setting condition

- Is it a particular method or common problem on more than one method?
- Can the problem be traced to setting parameters?
  - Sample pipetting volume
  - Reagent pipetting volume
  - Wavelength
  - Measuring point
  - Method (Rate, End, Fixed, Sample Blank)
  - Position
  - ID barcode
  - R1 & R2
  - Bottle size

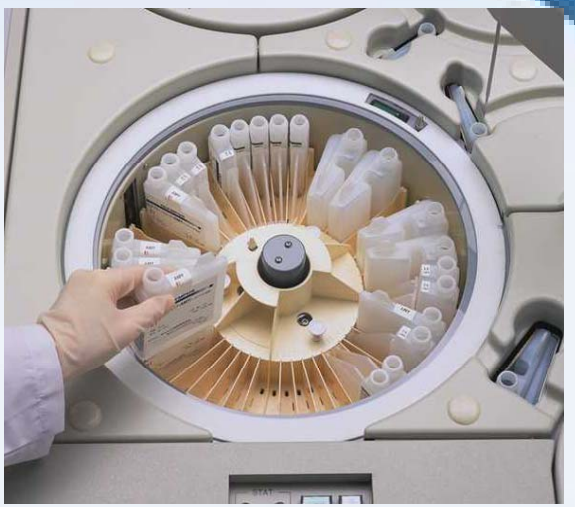


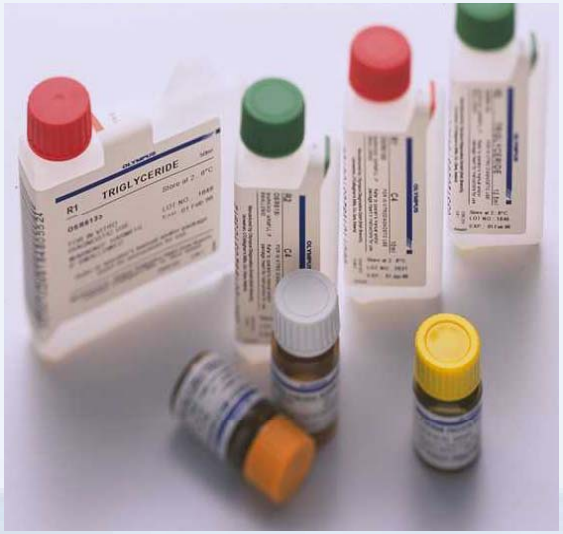


# 2. Reagent condition

Storage/alteration

- Visible appearance
  (colour, dirt, bubble, sediment, bacterial growth)
- Temperature,
- Contamination,
- Lot no.
- Expiry date.





# 3. Instrument condition

- Detergent

Wash solution,

Concentration,

Crystal,

Periodic maintenance (daily, weekly, monthly and preventive)

- Water quality

Conductivity,

pH,

Water filter (dirty, clogged),

Inlet water temperature

# 3. Instrument condition

- Water quality

It is desirable to have a system which has the capability of using several proven water purification technologies -

Reverse osmosis,

Ion exchange,

Micro-filtration and

Photo-oxidation.

# 3. Instrument condition

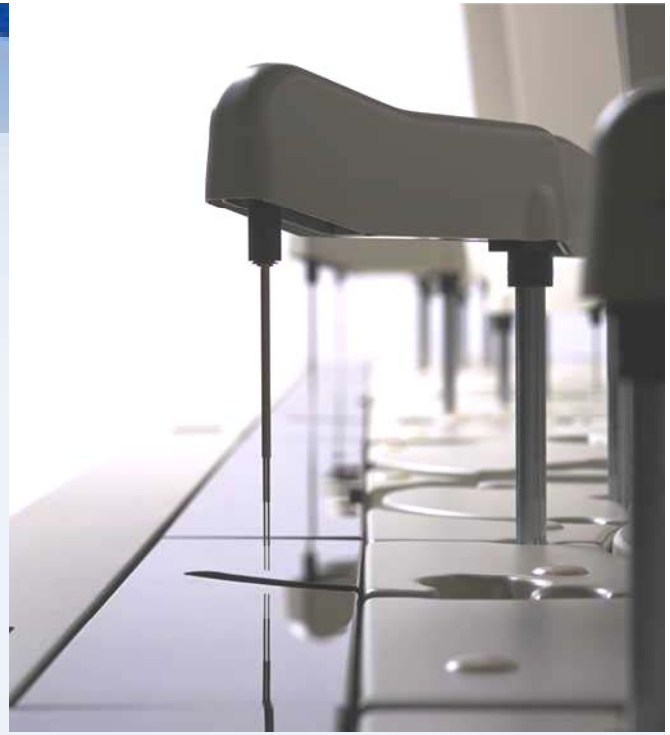
- Sample pipetting /Reagent pipetting

  - Sample/Reagent probe condition

    Dirty, bent, change of shape, position, deterioration of dispense

  - Sample/Reagent syringe condition

    Smooth action, condensation, noise from syringe unit, air in line (Pinhole, Crack or Connection)



# 3. Instrument condition

- Mixing bar condition

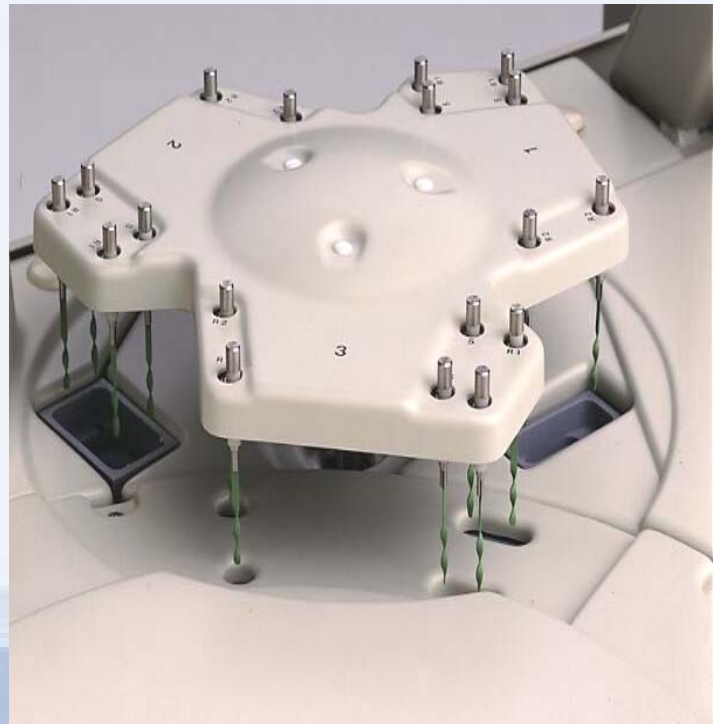
  Attachment, dirty, teflon peel, position, shape, surface scratch, inspection of rotation condition (noise, bias).

- Washing station for mix bar,

  Sample probe & reagent Probe

  Sufficient volume of washing water

  Dirt and crystallization.



# 3. Instrument condition

- Cuvette washing

temperature, water drop, overflow, change of detergent, nozzle blockage, crystallization, Fingerprint, Dirty, Wet outside.

- Lamp & light path

Lamp - Stability (photocal, water test, dye test)

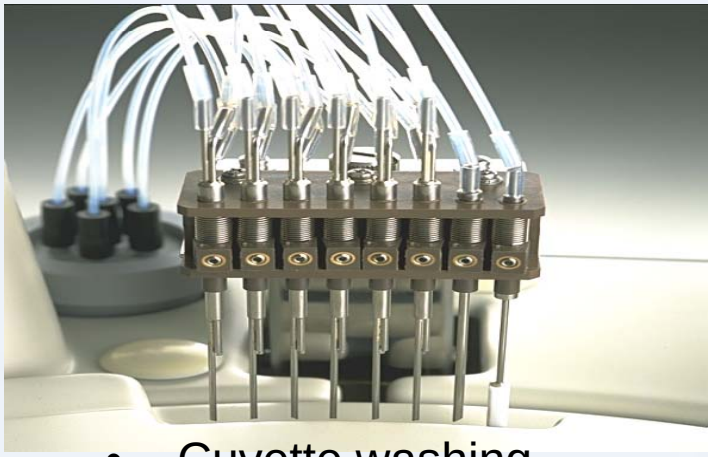
Light path - dust, wet lens

Cuvette holder - dust, wet

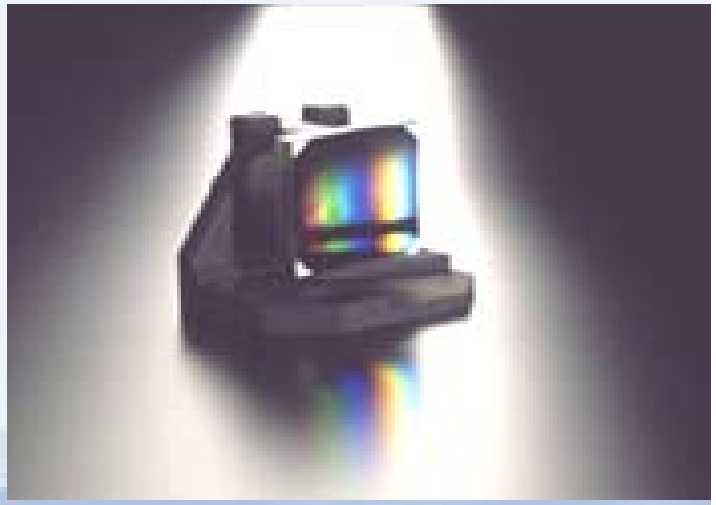
- Tank of deionized water

Tank - sediment, slime, fungal, dirt

Water - bubble, colour



- Cuvette washing



- Lamp & light path

# Preventive Maintenance Program

- Follow manufacturer's instructions for calibration of instruments.
- Read and understand instructions for routine instrument care.
- Perform all preventive maintenance provided by manufacturer's instructions.
- Keep all spare parts available for immediate use.
- Record name, address, and phone number of a contact person for maintenance or repair.
- Create a maintenance form or use the one provided.

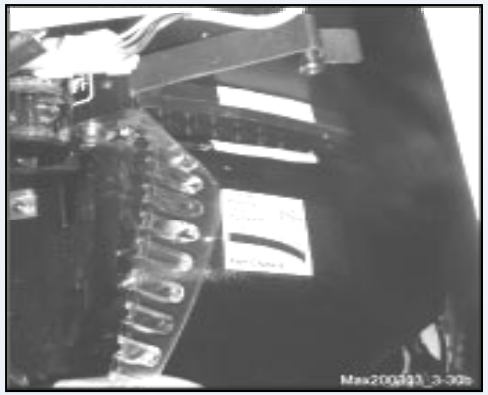
# Carryover

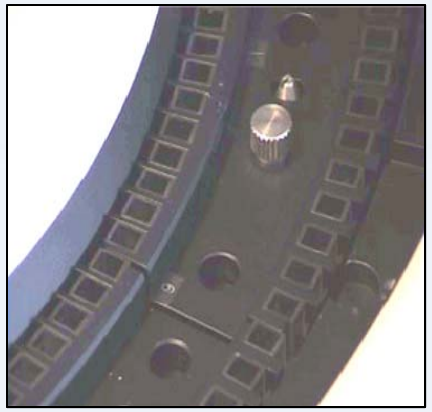
Carryover can occur on

- a sample probe or reagent probes,
- in reusable cuvettes or in systems using disposable cuvettes — as a result of residual specimen in the pipetting system.

# Carryover

- Discrete clinical chemistry analyzers use separate reaction cuvettes, cells, slides, or wells which are disposed off following chemical analysis.



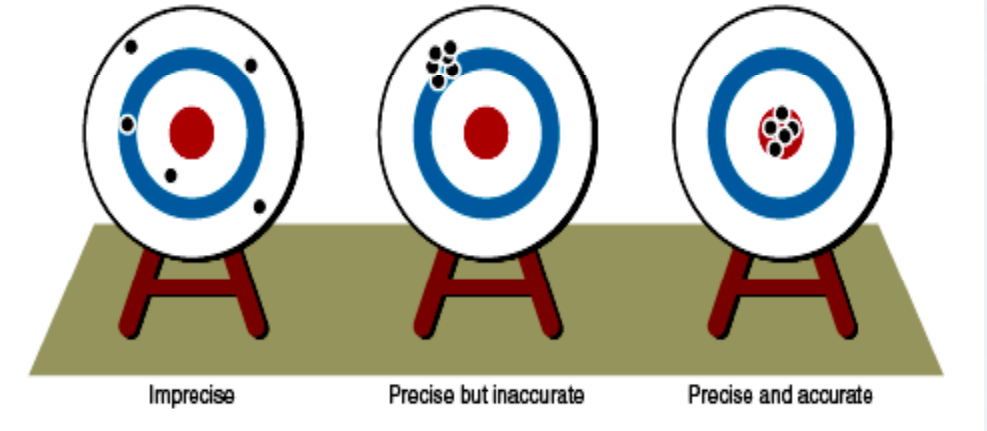


- This keeps sample and reaction carryover to a minimum but increases the cost per test due to disposable products.

# Precision

Precision check is must after the trouble shoot

Precision refers to the reproducibility of a result.
Checking precision is required while :
-Calibration
-Troubleshooting.




## Precision

*How well a series of measurements agree with each other*

Precision check - Any sample material /control material with known value can be used.
CV % less than 5 shows that the methods are precise.

# Conclusion

- The impact of the ever-changing technology in regard to responsibilities and training therefore needs continual appraisal.

- The goal of a successful automation must be to change the way in which work is done in the laboratory and this involves changing not only the tools and processes, but also the job structure and ultimately the way people think about their work

# Final Thought

"There are many challenges the clinical laboratory personnel face. But there is no doubt that automation is making an impact on the diagnosis and treatment of patients now and will be increasingly so in the future."

***When a system is not working for patients,***

***trying harder will not work.***

***Only changing the care system or our***

***approach to care will work.***

***THANK YOU !***