

Worksheet for QC of AHG (anti IgG + anti C3d)

| Parameters  | Required quality control criteria (DGHS) | Name of the firm |  |  |  |
|---|--|------------------|--|--|--|
|   | Date of Manufacture                      |                  |  |  |  |
|   | Date of Expiry                           |                  |  |  |  |
|   | Lot No.                                  |                  |  |  |  |
|   | Quantity                                 |                  |  |  |  |
| <b>Appearance</b><br>▪ Turbidity<br>▪ Precipitate<br>▪ Particles  | No<br>No<br>No                           |                  |  |  |  |
| <b>Specificity Agglutination with</b><br>▪ O Positive unsensitized cells<br>▪ O Positive sensitized cells | No<br>Yes                                |                  |  |  |  |
| <b>Reactivity</b><br>▪ Prozone  | No                                       |                  |  |  |  |
| <b>Potency (titre)</b><br>▪ O+ve anti D (IgG) sensitized cells  | 1:64                                     |                  |  |  |  |
| <b>Fulfilling DGHS criteria</b>   |  |                  |  |  |  |

QC of Normal Saline

| Parameter   | Quality Requirement      | Frequency |
|---|--------------------------|-----------|
| Appearance  | No turbidity / particles | Daily     |
| pH  | 6.8 to 7.4               | New batch |
| 1 ml saline + 1 ml 5% RBC, centrifuge for 10 min. Observe for hemolysis | No hemolysis             | New batch |

## Reagent Red Cell Panels

### What are reagent red cell panels?

- Red cell suspensions used in tests employing the principles of hemagglutination and hemolysis for the detection and identification of blood group antibodies.

- Sources { Commercial  
In-house { Regular local donors  
Staff members/volunteers

### Applications of Reagent Red Cells

- Reverse ABO grouping
- Antibody screening
- Antibody identification
- Antibody titration
- Allogeneic adsorption
- Preparation of Check cells

(Please refer to Annexure - H)



## CHAPTER 19

### Quality control of blood components (QC Components)

Quality control of blood components is an integral part of the quality management systems in Blood bank. Quality assurance ensures proper yield, functionality and efficacy of the components for patient care. Quality control of components is defined as testing of random components to ensure they achieve reliably specific standards. It should include analysis of test results and detection of irregularities to identify deficiencies in production of Blood & Blood Components.

#### Quality requirements for Component preparation:

Quality in Blood Components be achieved only if all aspects of blood collection, component preparation, testing, storage and transport are controlled and monitored.

- Blood bank should conform to accommodation and environment standards as per regulation, the ambient temperature of blood component processing areas should be maintained within a range that should not have an adverse affect on component viability/shelflife
- Blood bank should conform to specifications for blood components, equipment, and materials as per laid down national standards.
- Staff should have knowledge, understanding of standard operating procedures (SOP) of component preparation.
- Blood bank should ensure validation of processes, procedures, equipment, and materials. It is important that quality control procedures should be properly validated before implementation.
- Regular maintenance schedule for equipment management and calibration
- Documentation of all processes and procedures for traceability
- Ensure availability of Procedures for prevention of microbial contamination
- Training of staff
- Staff health and hygiene
- Monitoring of all activities to ensure continuous quality improvement.

#### Factors that affect quality of components :

Component preparation involves number of processes and procedures and the key factors that affect the quality of final output of components are :

- 1. Donor selection :** Donor should not be on antiplatelet drug therapy, if so defer for defer for 72 hours for better platelet yield. Donor weight is also important for donor selection.
- 2. Quality of blood bag and anticoagulant** preservative solution used determines the quality of components as gaseous exchange depends on the properties of the bag. The storage length of components also varies with the type of blood bag and anticoagulant used, such as shelf life of platelet 3/5 days.

### 3. Techniques of phlebotomy

- Venipuncture should be clean, there should be no double prick, minimal tissue trauma for better yield of components.
- Flow should be continuous, uninterrupted and completed within 8-10 min. Prolonged draw time of 15 to 20 minutes is not suitable for platelet or plasma products.
- There should be frequent gentle mixing of the bag to avoid any clotting. Automated blood mixers reduce interruption in mixing of the blood bag.

4. **Over/under collection** of a unit of blood alters the ratio of blood to anticoagulant which affects storage of RBCs.

5. **Time period of separation of components** – Component separation should be started within 8 hrs of collection. Time limits during which leukocyte reduction should take place for pre storage leukocyte-reduced RBCs. Faster Freezing of plasma allows improved recovery of coagulation Factor VIII.

6. **Transit temperature:** should be 20-24°C for not more than 8 hours.

7. **Refrigerated centrifuge:** Critical variables such as speed, acceleration, deceleration rates, temperature, duration of centrifugation, maximum g-force achieved, balancing of centrifuge cups, degree of braking affect the red cell sedimentation process.

Preparation protocols for optimum conditions should be determined and maintained for refrigerated centrifuge. The refrigerated centrifuge should be validated, maintained and calibrated for the best yield and consistency in quality of component as these are dependent on the processing conditions.

8. **Storage temperatures of components** should be as per standards and maintained with documentation. Uninterrupted, gentle flat bedded platelet incubator/agitator for controlled mixing of platelets during storage ensures viability of platelets

9. **Automated methods** reduce variability in red cell contamination of platelets and permits increased extraction of plasma. Buffy-coat removal allows reduction in leukocytes in cellular components.

10. **QC of Equipment** is necessary for components to achieve desired properties in a consistent manner during component preparation.

**Essential Quality Elements:** that govern quality control of blood components include sampling and the criteria laid down for quality control for different components.

1. BTS should have laid down policies for sampling techniques, Quality control testing should be performed to verify conformance of the product characteristics with defined specifications based on minimum standards and regulatory requirements for key parameters of each component type.
2. The frequency of quality control testing should depend on the volume of blood components produced. It should be performed on at least 1% of all components produced per month for all parameters to be measured. If fewer than 100 per month are prepared, then at least 4 units should be tested/month. 75% or more of components monitored must meet specifications.

### Volume of blood in blood bag

$$\text{Vol (ml)} = \frac{\text{Weight of bag + blood components(g)} - \text{wt of empty bag}}{\text{Specific gravity of component}}$$

#### Specific gravity

- Packed RBC = 1.093
- Platelets = 1.035
- Plasma = 1.030
- Whole blood = 1.050

Volume should be recorded on all units with appropriate labels. Parameters used for the volume and yield of components directly depend on the volume of whole blood collection.

### Standardized procedures for Sampling

BTS should practice non-destructive sampling methods involving use of pack tubing. Sampling methods should be validated to ensure that they produce consistent samples, regardless of the operator. Standardised SOP's for mixing of products and stripping of lines should be developed as these are vital for quality results.

### When should QC be done

- As per standard schedule of SOP and on specific indications as following
- For platelet products it should be done on expiry date (end of storage period) of the component.
- On installation and after repair of equipments (refrigerator, centrifuges, deep freezers etc.)
- Modification in procedure for components preparation.
- Recruitment of new personnel.

### Whole blood:

- Frequency of control: 1% of all units with minimum of 4 units per month
- Storage :- 2°C to 6°C, for CPDA-1 the storage time is 35 days, CPD & CD2D – 22days.

### QC of whole blood

| Parameter     | Quantity Requirement  | Frequency of control           |
|---------------|-----------------------|--------------------------------|
| Volume        | 350/450 ml $\pm$ 10%  | 1% of all units                |
| Anticogulants | 49/63 ml              | All units                      |
| PCV (Hct)     | 30 to 40%             | 4 units per month              |
| HBsAg         | Non Reactive by ELISA | All units                      |
| Anti-HCV      | Non Reactive by ELISA | All units                      |
| Anti-HIV 1/2  | Non Reactive by ELISA | All units                      |
| Syphilis      | Negative by Screening | All units                      |
| Sterility     | By culture            | Periodically (1% of all units) |

### QC of Red cell concentrate from 450ml blood bags

| Parameter | Quantity Requirement | Frequency of control |
|-----------|----------------------|----------------------|
| Volume    | 280 +40              | 1% of all units      |
| PCV       | 70%+5%               | Periodically         |
| Sterility | Culture              | Periodically         |

### QC of Red cell concentrate in preservative solution (Adsol/SAGM)

| Parameter | Quantity Requirement | Frequency of control |
|-----------|----------------------|----------------------|
| Volume    | 350 $\pm$ 20         | 1% of all units      |
| PCV       | 60% $\pm$ 5%         | Periodically         |
| Sterility | Culture              | Periodically         |

### QC of Fresh Frozen Plasma

| Parameter                  | Quantity Requirement     | Frequency of control |
|----------------------------|--------------------------|----------------------|
| Volume                     | 200 - 220 ml             | 4 units / month      |
| Stable Coagulation Factors | 200 units of each factor | 4 units / month      |
| Factor VIII                | 0.7 units / ml           | 4 units / month      |
| Fibrinogen                 | 200 - 400 mg             | 4 units / month      |

### QC of Cryoprecipitate

| Parameter               | Quantity Requirement     | Frequency of control |
|-------------------------|--------------------------|----------------------|
| Volume                  | 10 - 20 ml               | Occasionally         |
| Factor VIII             | 80 - 120 units           | Occasionally         |
| Von - Willebrand factor | 40 - 70% of the original | Occasionally present |
| Factor XIII             | 20 - 30% of the original | Occasionally         |
| Fibrinogen              | 150 - 250 mg             | Occasionally         |
| Fibronectin             | 55mg                     | Occasionally         |

### QC of Platelet concentrate from 450 ml whole blood

| Parameter         | Quantity Requirement              | Frequency of control |
|-------------------|-----------------------------------|----------------------|
| Volume            | 50 - 70 ml                        | All units            |
| Platelets count   | $>5.5 \times 10^{10}$             | 4 units per month    |
| pH                | $>6.0$                            | 4 units per month    |
| RBC contamination | 0.5ml                             | 4 units per month    |
| WBC contamination | $5.5 \times 10^7 - 5 \times 10^8$ | 4 units per month    |

### QC of Platelet concentrate from buffy coat

| Parameter         | Quantity Requirement  | Frequency of control |
|-------------------|-----------------------|----------------------|
| Volume            | 70 - 90 ml            | All units            |
| Platelets count   | $>6.9 \times 10^{10}$ | 4 units per month    |
| pH                | $>6.0$                | 4 units per month    |
| RBC contamination | Traces to 0.5 ml      | 4 units per month    |
| WBC contamination | $5.5 \times 10^6$     | 4 units per month    |

### QC of Apheresis Platelet

| Parameter         | Quantity Requirement        | Frequency of control |
|-------------------|-----------------------------|----------------------|
| Volume            | 200 - 300 ml                | All units            |
| Platelets count   | $>3.0 - 7.0 \times 10^{11}$ | 4 units per month    |
| pH                | $>6.0$                      | 4 units per month    |
| RBC contamination | Traces to 0.5 ml            | 4 units per month    |
| WBC contamination | $5.5 \times 10^6$           | 4 units per month    |



All Platelet units should show 'swirling' effect. Absence of swirling in platelet concentrates is highly predictive of poor post-transfusion platelet count increments and increased risk of bacterial contamination'

**Calculation for Platelet count from RDP**

$$\begin{aligned}
 \text{Platelet Count in bag} &= \text{Concentration} \times \text{Volume} \\
 \text{Concentration} &= 1100 \times 10^9 / \text{L} \\
 &= 1100 \times 10^9 / 1000 \text{ ml} \\
 1000 \text{ ml} &= 1100 \times 10^9 \\
 50 \text{ ml} &= ? \\
 &= \frac{50 \times 1100 \times 10^9}{1000} \\
 &= \frac{50 \times 110 \times 10^{10}}{1000} = \frac{5500 \times 10^{10}}{1000} \\
 &= 5.5 \times 10^{10} \text{ per bag}
 \end{aligned}$$

**RBC Contamination**

No pink/red discoloration on visual inspection = insufficient red cells to cause immunization

$$\begin{aligned}
 \text{MCV of RBC} &= 90 \text{ m}^3 \sim 100 \text{ m}^3 = 10^2 \text{ m}^3 \\
 1 \text{ ml} &= 1 \text{ cc} = 1 \text{ cm}^3 = 1 \times (10 \text{ mm})^3 \\
 &= 1 \times 10^{12} \text{ m}^3 \\
 0.5 \text{ ml} &= 0.5 \times 10^{12} \text{ m}^3 \\
 &= 0.5 \times 10^{10} \times 10^2 \text{ m}^3 \\
 &= 0.5 \times 10^{10} \text{ RBCs} \\
 &= 5 \times 10^9 \text{ RBCs}
 \end{aligned}$$

**Quality control of Equipments of Component Lab**

**Refrigerated Centrifuge** - Daily checklist for equipment should be filled up .

- Buckets & centrifuge bowls should be cleaned with warm water and mild detergent. In case of spill/breakage of (blood) use 1% Na hypochlorite to clean and decontaminate.
- Should be calibrated upon receipt, repairs or in case of low platelet yields
- Preventive Maintenance should be done regularly as per schedule for
  1. Calibration of speed with a tachometer (twice a year)
  2. Cleaning and lubrication of motor
  3. Regular change of worn out carbon brushes

**Cryoprecipitate Bath/Water Bath**

1. Temperature should be checked and recorded daily.
2. Water should be changed once a week or if there is any leakage
3. Recalibrate temperature controller whenever the :

- Temperature probe/ circuit board is replaced
- Digital display & certified thermometer show difference in temperature

#### 4. Platelet Agitator

- Temperature should be checked and recorded daily
- Periodic cleaning & lubrication during Preventive Maintenance
- Platelet Agitator should be calibrated at 60-70 strokes /min

#### **Quality control of Blood storage Equipment**

- Daily temp check of Refrigerators, Freezers & Platelet Incubator
- Visual and audio alarms check on regular basis
- Check monitoring device / THERMOGRAPH (continuous temperature recorder) display and maintain documents for the same.
- Temperature check at different locations in larger equipments.
- Actual temperature checks with Hg thermometer in glycerol.
- Alarm test to be done with sensor dipped in a beaker with tap water / ice slush.

#### **Quality Control Monitoring of Components:** Quality monitoring is necessary for

1. Regulatory and/or accreditation requirements for minimum blood component standards.
2. It should be used to identify supply of sub-optimal reagents and variations from validated standard operating procedures by analyzing trend data for early drift or deviations.
3. Quality monitoring involves the regular and systematic review of quality control data and compliance with defined specifications.
4. The timely detection of QC failures should provides a proactive approach to early identification and resolution of complaints.
5. To take essential action at defined threshold level of established specifications.

#### **Documentation :**

- SOP 's for Component preparation
- Equipment checklists-Daily monitoring
- Records of PM/AMC/CMC
- Calibration and Validation records
- QC records of packed red cells, platelets (PRP-PC & BC-PC), AP-PC, FFP and cryoprecipitate

**(Please refer to Annexure - I)**



## CHAPTER 20

### Quality control TTI Testing

A quality orientated approach is essential for TTI screening in blood bank in order to provide safe and effective product at all times.

TTI screening of donated blood and the quarantine of blood and blood components are critical processes that should be followed to ensure safe blood for transfusion. Blood should either be released for clinical use or be discarded on the basis of screening tests.

As per the Drugs and Cosmetics Act of India, mandatory tests for screening of blood donation include

- Anti-HIV 1 & 2 antibodies
- Anti-HCV antibodies
- Hepatitis B Surface Antigen (HBsAg)
- Treponema pallidum (Syphilis)
- Malaria

### Implementation of QC for TTI

1. Establish written policies and procedures
2. Design forms and flow charts
3. Select high quality controls
4. Perform statistical analysis
5. Set target values (mean, SD)
6. Establish Levey - Jennings charts
7. Routinely plot control data
8. Establish and implement troubleshooting and corrective action protocols
9. Establish and maintain system for documentation
10. Train all staff

#### 1. Establish written policies and procedures

Blood bank should define policies and procedures for TTI screening on blood samples collected at the time of blood donation. The basis for any quality system is that procedures are documented, monitored and recorded.

Procedures should also include correct labeling to ensure correct identification throughout the screening process. Blood bank should also have appropriate systems for linking all test results to the correct donations and donors so that donors' records can be reviewed each time they come to donate. These Quality management systems in place should ensure that correct results are allocated to each donation and prevent errors resulting in the transfusion of an unsafe unit.

The STANDARD OPERATING PROCEDURES for TTI lab should be developed in the blood bank as a set of instructions to be followed at all times by all staff for :

1. Reception and handling of samples
2. Performing the assay
3. Use and maintenance of the Elisa washer
4. Use and maintenance of the Elisa reader
5. Use and maintenance of the pipettes
6. Issuing the results
7. Retrieving and disposing of positive donations
8. Cleaning and decontaminating the laboratory.

## **2 Design forms/checklists**

Blood bank should develop checklists /worksheets, for each assay detailing all the required actions in the correct sequence. After the screening, the completed worksheet becomes the quality record of that batch of testing and should complete the quality circle providing traceability.

### **Essential components for quality control(QC)**

Quality control in TTI lab denotes the consistent measures undertaken for each TTI assay to ensure that the test should work accurately as per the limits of the test to produce valid and acceptable results. This indicates that the test should be valid, all test conditions for that run should be met and all test results for that run are reliable.

### **Elements of QC for TTI**

- Internal QC covering the reagents and techniques.
- Assessment on specificity and sensitivity
- Batch pre acceptance testing of new batches of kits
- External quality checks (confirmation of +ve findings)
- External Quality Assessment

### **Selection of assays**

Sensitivity and specificity are the key factors to be considered in selecting a specific assay. For the screening of blood donations, both sensitivity and specificity should be the highest possible or available.

### **Sensitivity**

Sensitivity is the probability that the test result will be reactive in an infected individual. The sensitivity of an assay is therefore its ability to detect the weakest possible positive sample.

**Specificity** is the probability that a test result will be non-reactive in an individual who is not infected: the specificity of an assay is its ability not to detect false or nonspecific positives.

### **Calculation of the sensitivity and specificity of an assay**

True TTI status

Assay results    Positives    (a) True-positives + (b) False-positives

Assay results    Negatives    (c) False-negatives + (d) True-negatives

Compare your result with the sensitivity given in the manufacturer's instructions.

$$\text{Sensitivity} = \frac{a}{a+c} \times 100\%$$

$$\text{Specificity} = \frac{d}{b+d} \times 100\%$$

The sensitivity and specificity of assays are generally inversely related; that is, as the sensitivity is increased, the specificity decreases and as the specificity is increased, the sensitivity decreases.

### **Predictive Values**

Predictive values are another way of looking at the performance of the assays i.e what can be expected from the assay.

The positive predictive value (PPV) and negative predictive value (NPV) are measures of the actual performance of an assay in blood bank.

The positive predictive value is the probability of a positive result being a true positive. The negative predictive value is the probability of a negative result being a true negative.

$$\text{PPV} = \frac{a}{a+b} \times 100\%$$

$$\text{NPV} = \frac{d}{c+d} \times 100\%$$

The use of rapid assays is generally not recommended for blood screening as they are designed for the immediate and rapid testing of small numbers of samples. These are manual assays and lack in permanent records and traceability. They should be used in laboratories with medium to high throughput or in smaller blood centers that have limited resources. They should be appropriate when a blood bank needs to screen specific donations on an emergency basis for immediate release of products due to a critically low blood inventory or when rare blood is required urgently or to screen before an apheresis donor in emergency.

### **Important points for consideration prior to use of kits and performing the assays:**

- Mandatory to use licensed /CDSCO (Govt. of India) approved kits
- Mandatory to use kits before expiry date

**Follow strictly the Physical parameters as incubation time, reagent concentration, temp range mentioned on the test insert**

- a. Kits and samples should be brought at room temp. before use
- b. Wells of the plate should not be touched with micropipette tip
- c. Always use tips compatible and recommended with the micropipette
- d. Controls and unknown samples should be treated in similar manner
- e. Reagents from one kit should not be mixed with another

### **Internal and External Controls**

Each test run must include one full set of controls that yield results within the limits of standard for acceptability and validity.

Any test run NOT having at least minimum no. of controls within acceptable range IS INVALID and must be repeated. There are two categories of controls Internal/Kit controls and External controls.

#### **Internal/Kit controls**

- Set of controls provided with the kit- both positive as well as negative
- Should be used with the same batch only
- These do not detect any minor deterioration of the kit

#### **External controls**

These can be procured from National reference centres, commercially as control panels and can be prepared in house from reactive/non reactive blood bags

#### **Set of controls included from outside**

- Positive samples -borderline positive and negative
- Should be used with the same batch only
- These detect any minor error in the assay performance

#### **Validity criteria of test run**

- Internal controls (positive & negative) and Blank value should be within prescribed limits
- Cut-off of test run should be calculated as per kit insert
- External controls (borderline positive & negative) should give valid results

#### **Interpretation of Results**

- Samples OD at or above the cut-off value - Reactive
- Samples OD below the Cut-off value - Non-reactive

**Grey zone samples:** Those below the 10% of cut off are in grey zone. These should be repeated in duplicate:

- If one or both above cutoff                      Reactive
- If both value below cutoff                      Non-reactive

#### **Preparation of Borderline External Positive Control (NACO guidelines):**

1. Done for in-house preparation of borderline positive control (borderline reactive)

2. Used in serological assays by ELISA for HIV, HBV, HCV etc
3. Perform this only if system is stable
4. Finding the suitable Dilution for Borderline Control
  - a) Calculate the Cut-off value (from the package insert)
  - b) Select a high titre plasma/serum from your positive samples
  - c) Select a negative sample for dilution
  - d) Prepare two-fold serial dilutions depending on the positivity.
  - e) Test each dilution in the same run for the particular assay for which the QC is being prepared.
  - f) Note down the ODs.
  - g) Calculate E ratio (=sample OD/Cut off OD).
  - h) The result usually shows a sigmoid curve.
  - i) An appropriate dilution between E-ratio - 1.5 to 2.0 (Indirect/competitive ELISA) and 0.7 to 1.0 (Sandwich ELISA) should be selected from the linear position of the curve as the Borderline Control.

#### **Batch Validation should be done to**

- Determine degree of inter aliquot variation.
- Check the batch has been sufficiently mixed and is homogenous so as to minimize the inter aliquot as well as inter run variation.
- Accept the batch if samples show minimal variation and yield the target titer after aliquoting

#### **Large batch production:**

- a) Centrifuge the selected sample at 3500 rpm for 10 minutes.
- b) Prepare required amount of bulk dilution as per requirement e.g. if dilution selected is 1:256 and required quantity is 25 ml, then dilute 100  $\mu$ L positive specimen in 25.5 ml negative specimen (diluent).
- c) Mix properly.

#### **A. Batch validation: E. Ratio**

- a) Run the prepared QC sample in duplicate
- b) Calculate the average.
- c) Ascertain the average E- ratio is between 1.5 and 2.00 (Indirect/competitive ELISA) and 0.7 to 1.0 (Sandwich ELISA)
- d) An appropriate dilution should be selected from the section of the graph where results variability can be followed i.e. linear position of the curve.

#### **B. Batch validation: Homogeneity/ Repeatability:**

- a) Once the batch has been dispensed into smaller volumes, a specimen from each of the aliquots



must be tested to ensure that each aliquot will produce the same results, the batch is reproducible and homogenous.

- b) Randomly select 10 to 20 aliquots as per lab policy
- c) Test each of them same day/ in 2-3 days as per lab policy
- d) Batch is acceptable if CV < 15%.

#### Using the aliquots as QC for method performance (imprecision) study

- a) Set mean and SD and place them on the LJ graph
- b) Daily run QC sample along with routine specimens.
- c) Monitor Levy-Jennings control chart in daily runs.

**Statistical Analysis of QC data** : is important for monitoring quality assurance of TTI testing. Need data set of at least 20 points, obtained over a 20 day period to calculate mean, standard deviation and develop Levey - Jennings charts.

Tools required for data management for calculations and analysis are

- a. Knowledge of Basic statistics skills
- b. Use of Manual methods
  - Graph paper
  - Calculator

Use of Computer software

- Spreadsheet
- Important skills for laboratory personnel

#### Calculation of Mean: ELISA Tests

- Collect optical density (OD) values for Controls for each assay run.
- Collect cutoff (CO) value for each run.
- Calculate ratio of OD to CO (OD/CO) for each

Use these ratio values to calculate the Mean, SD and CV%

$$\text{Mean} = \frac{\sum X}{n}$$

(Sum total of E ratio)  
(Number of reactivity)

**Standard deviation** is calculated as Comparison of each of the individual values (E ratio) with the mean (X) to find out the deviations from the mean.

If the E ration is x1 then the deviation will be X1 - X which is expressed as 'd'. The deviations are then squared.

These squared deviations are added and expressed as  $\sum d^2$  or  $\sum (X_n - X)^2$  or The result is then divided by the number of readings.

- The square root of the above value is taken to find out

$$SD = \frac{\sum (X_n - \bar{x})^2}{n}$$

**Co Efficient of Variation** is expressed as the percentage and the following formula is used.

$$CV (\%) = \frac{SD \times 100}{\text{Mean}}$$

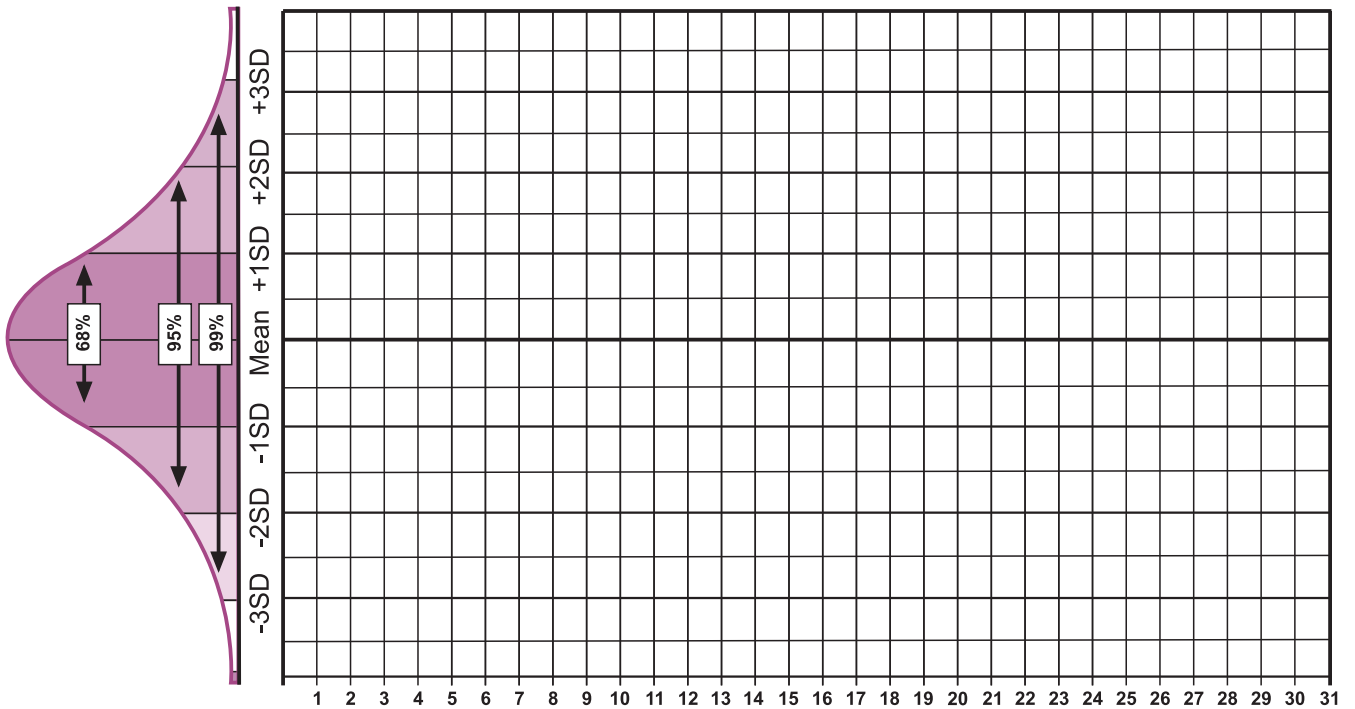
CV less than 10% is considered as an indication of little variation

### Monitoring of QC

- Use Levey-Jennings chart
- Plot control values each run, make decision regarding acceptability of run
- Monitor over time to evaluate the precision and accuracy of repeated measurements. The closeness of measurements to the true value is indicative of the “accuracy” of the assay and the degree of fluctuation in the measurements is indicative of the “precision” of the assay
- Review charts at defined intervals, take necessary action, and document

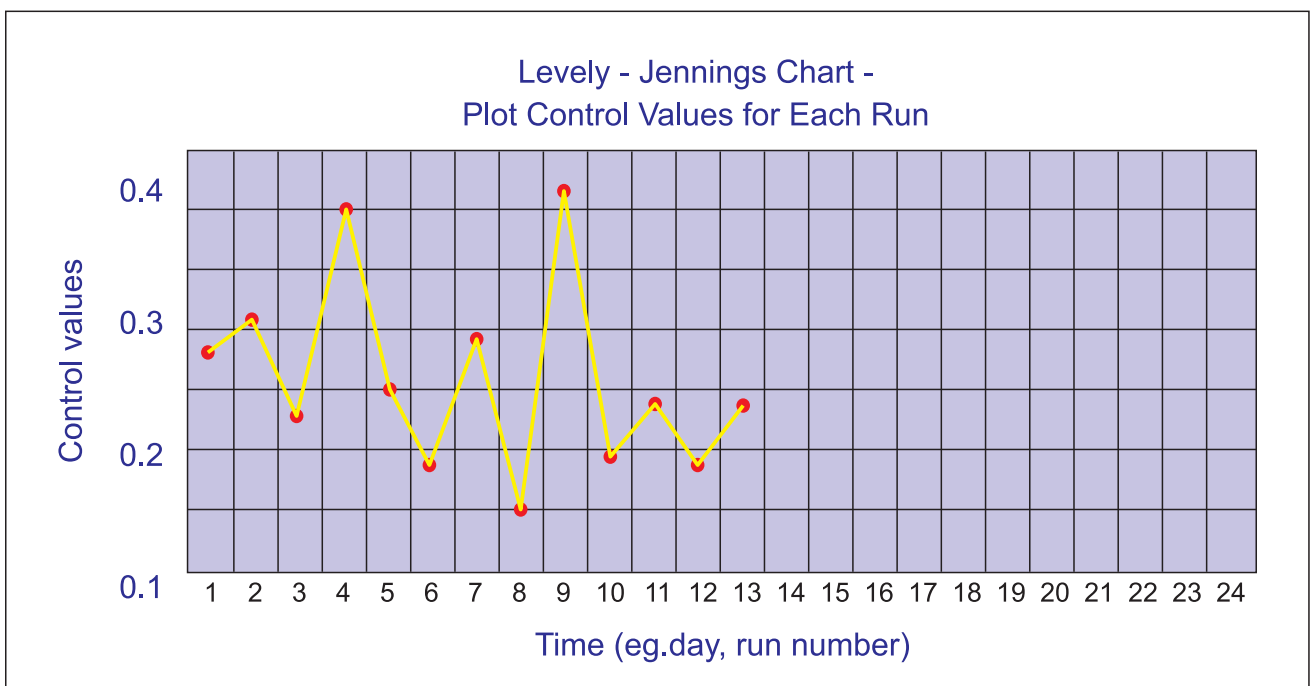
**Levey - Jennings chart** is an invaluable tool used in any TTI lab that is using ELISA as the screening test.

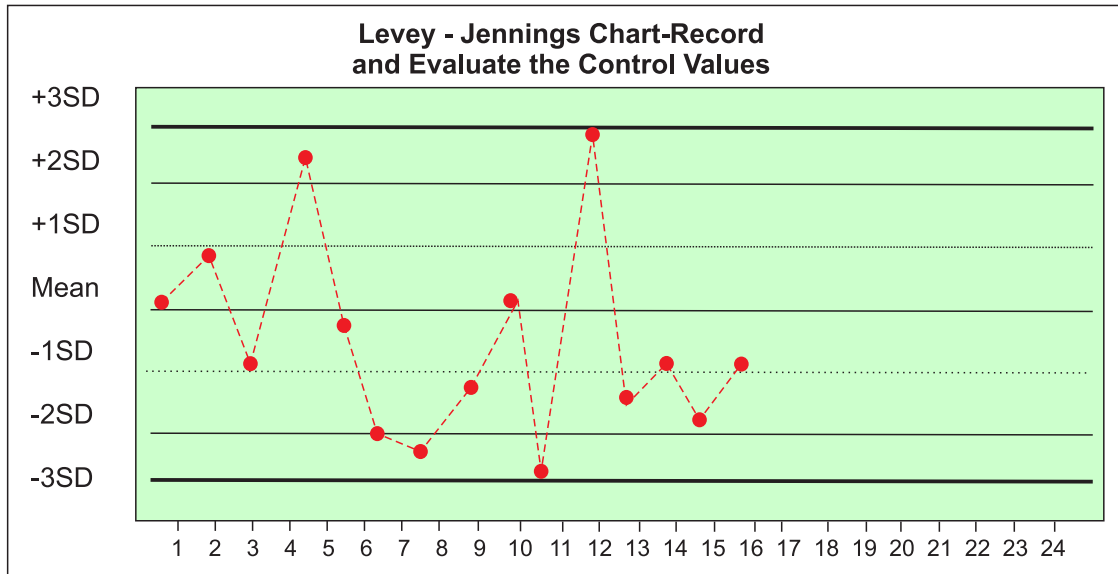
- Ideally you should have at least 20 data points to define your Mean and SD to define your Range.
- Calculate Mean, SD, Range.
- Now take chart and label X-axis as Time period used for Run.
- Label Y-axis as Control values (Mean & SD).
- Scale and label the Y-axis from lowest to highest expected control values so that:the mean is located at the center of your graph.
- SD is the numerical value applied in an increasing/ decreasing fashion on either side of the mean, to denote  $\pm 1$  SD,  $\pm 2$  SD,  $\pm 3$  SD, numerical values.
- Write the numerical values obtained for  $\pm 1$  SD,  $\pm 2$  SD,  $\pm 3$  SD,  $\pm 4$  SD next to the correct label on the chart.
- Draw lines for mean and SDs
- Begin plotting analyzed QC results.



In general, the  $\pm 2$  SD is the criteria for the limits of the acceptable range for a test. When the QC measurement falls within that range, there is 95.5% confidence that the measurement is correct. If not the test results for that run are not valid. Test is invalid also if SD is beyond 2SD/One External control beyond 3SD or External Control values exceeds SD in 2 consecutive tests.

Only 4.5% of the time will a value fall outside of that range due to chance; more likely it will be due to error. Over four to seven days if the E ratio is within  $\pm 2$  SD but shows gradual increase or gradual decrease, which means either kit or operator is faulty





### Application of Control charts

- Highlight the outliers (values outside +/- 2 SD)
- Reveal batch to batch variation
- Reveal operator to operator variation
- Changes in assay performance even when test runs are valid

### Scope of LJ Chart

Detection of the following

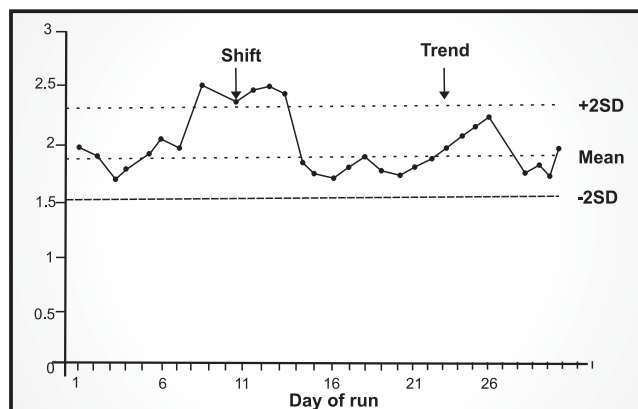
- Systematic variation
- Random variation
- Lot to lot variation
- Day to day variation

### Systematic variation

Systematic error is evidenced by change in the mean of the controls values. The change in the mean may be gradual or abrupt. It is termed as trend or shift.

**Trend**- Results change gradually in either direction indicating slowly changing parameters-deteriorating reagents, failing of equipment.

**Shift**-Results fall abruptly/sharply on one side of the mean indicating a major change has occurred.



## Interpretation of shift and trends

**Shift** - Control values of six consecutive runs fall on one side of mean. The possible causes ;

- Switching to new lot of kits
- New reagents
- Changes in incubation temperature
- New technical hand

**Trend** - Six consecutive points distributed in one general direction. The possible cause:

- Deterioration of reagents
- Deterioration of light source
- Gradual deterioration of calibration
- Slowly faltering equipment

## Random Variation

Random variation is evidenced by observance of one result significantly different from other results without any pattern could be due to:

- Transcription errors -mislabeling, data entry
- Sample mix-up - Errors in addition of samples to the plate - interchanging specimens
- Poor pipette precision
- Lack of equipment maintenance & calibration - Fungus on filters, volumes
- Elisa Reader not calibrated
- Poor technique as inconsistent washing
- Sudden change of staff / kit used in the BTS
- Lack of periodic training and following of SOPs/ manuals

## Documentation for quality control of TTI testing should include the following

- 1 The sample collection date.
- 2 The sample test date.
- 3 The identity of the test run in which each sample was included.
- 4 The identity of all samples in each testing run and a record of the position of these samples in any testing system.
- 5 The manufacturer, product number, lot or batch number and expiry date of the assay kits used.
- 6 The name of the operator and the supervisor.
- 7 The assay procedure.
- 8 The results obtained (eye-read and manually-transcribed results, if necessary).
- 9 The preparation of any reagents or buffer solutions used in the assay which were prepared in the laboratory.
- 10 The preparation and maintenance of any equipment used to perform the assay. If incubators are

used, temperature calibration checks should be included.

- 11 Temperature monitoring records for the laboratory itself (this is important if room-temperature incubations are required), incubators, water-baths and refrigerators used for the storage of assay kits or reagents.
- 12 Maintenance and calibration records for the equipment used, including any mechanical pipettes.
- 13 Records of the disposal of any positive donations, with details of the retrieval of the packs and any products prepared from them, and the actual destruction of the packs.

### **Training of all staff**

The most important part of quality control is training of all staff on SOP's, QC, and calculation of statistical values and plotting of the L. J charts. It should be an ongoing process with documentation.

**Please refer to Annexure - J**



## CHAPTER 21

### External Quality Assurance (EQA)

#### Quality in Blood Banks:

The primary goal of quality in blood transfusion services is 'transfusion of a safe unit of blood. Quality system applies to all aspects of transfusion practice from donor identification to appropriate clinical use of blood to ensure that the product or the tested unit of blood' is as safe as possible. Quality in blood banks can be achieved by strict adherence to quality control measures.

**Quality Control (QC):** Quality control (QC) is a procedure or set of procedures intended to ensure that the product or services adhere to a defined set of quality criteria or meets the requirements of the client or customer.

QC is similar to, but not identical with, quality assurance (QA). QA is defined as a procedure or set of procedures intended to ensure that a product or service under development (before work is complete, as opposed to afterwards) meets specified requirements.

- QC measures should be included during each assay run to verify that the test results are proper.
- QC is a technique used to detect and correct errors before they result in defective product or service.
- QC is a statistical process used to monitor and evaluate the analytical process that produces patient results.

#### Aim of QC:

The aim of quality control is to ensure that the results generated by the test are correct and meet the specified standards of safety and efficacy. QC includes statistical control procedures and also includes reagent and standard checks, linearity checks, etc. QC results should be used to validate whether the equipment is operating within pre-defined specifications, inferring that test results are reliable.

#### Quality Control:

QMS should describe methods of monitoring and evaluation of processes by its Blood Bank. In order to implement an effective QC program, blood bank should first decide which specific standards the product or service must meet. The extent of QC actions should be determined (for example, the percentage of units to be tested from each lot). QC procedures should be systematic and independent examination performed at defined intervals and at sufficient frequency to determine whether actual results comply with the expected results. Real data should be collected (for example, the percentage of units that fail) and the results reported to management personnel. After this, corrective action should be decided upon and taken (for example, defective units should be rejected). Finally, the QC process should be ongoing to ensure that remedial efforts, if required, have produced satisfactory results and immediately detect recurrences or new instances of trouble.



### **Internal Quality Control (IQC):**

Internal quality control in the blood bank involves a continuous, critical evaluation of the blood banks own methods and working routines. Internal QC for the blood bank should include evaluation of quality indicator data, targeted audits of a single process or system audits that are broader in scope and cover a set of interrelated processes. The results of the control program should be used as an important quality tool in daily work, The QC has to be part of a quality system and should be formally reviewed on a regular basis.

### **External Quality Assessment (EQA):**

External Quality Assessment (EQA) programs are invaluable tools used by blood bank/laboratories to periodically assess their analytical performance and achieve added confidence in reporting their test results or measurements. EQA should be designed to evaluate the overall performance and accuracy engaged in blood bank testing and monitor blood banks continual performance and improvement.

EQA in conjunction with daily QC assists Blood Bank in improving analytical quality, identify potential equipment or reagent failures and identify any training deficiencies.

### **Objective of EQA:**

Blood Bank should participate in external quality assessment with an objective to

- Monitor its performance and evaluate QC measures.
- Target to achieve excellence in each survey.
- Establish inter-Blood Bank comparability- Participating laboratory with the organizing laboratory by sharing of experiences and resolution of problems.
- Stimulate performance improvement to promote high standards of practice in Blood Bank.
- Encourage use of standard reagents/methodology for achieving quality results
- Ensure credibility of Blood Bank.
- Identify common errors.

### **Parameters under EQA in Blood Bank**

#### **TTI testing**

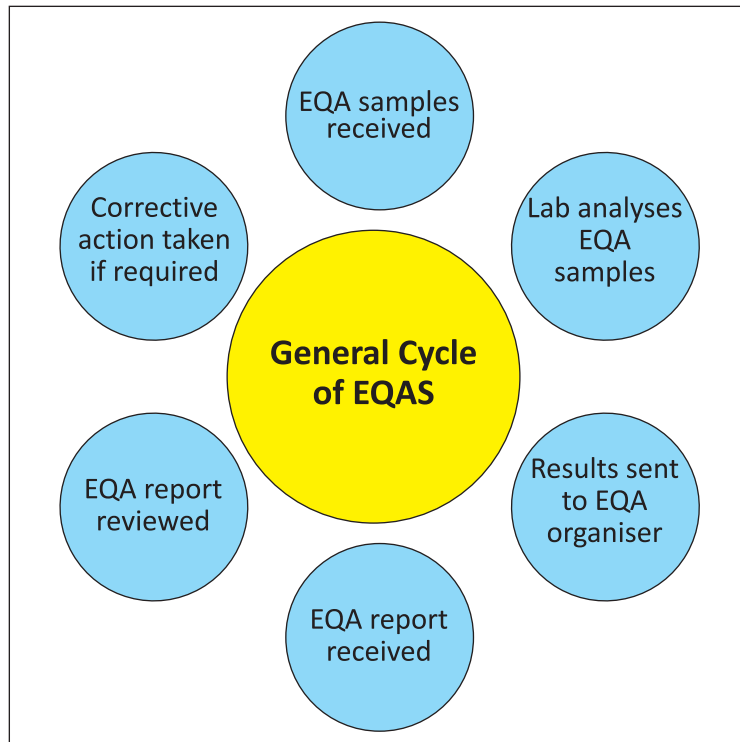
- HBsAg
- Anti- HIV 1&2
- Anti- HCV
- Syphilis (VDRL)
- Malarial Parasite

**Haematology** - Haemoglobin

**Immunohaematology** - Blood Grouping , Cross-match

### **Steps of analysis**

EQA is defined as a system for objectively checking the laboratory's performance using an external agency or facility. Careful preparation is required to participate in EQA with a specific achievable aim for each survey.



### What to look for in EQA

- Sample design & frequency
- Analytical goals
- Easy to read reports
- Scientific validity and reliability
- Education
- Scientific support

### Sample Design

- Appropriate matrix
- Stable, homogeneous material
- Appropriate concentration levels
- Appropriate frequency of testing

Samples received from organising blood bank/laboratory should be tested as part of routine work carried out by staff ordinarily responsible for and not necessarily by a senior experienced technician. The results should be communicated promptly by Blood Bank to the organising laboratory.

Analysis of results received from participants as per internationally acceptable statistical methods (including Mean, Standard Deviation (SD), Coefficient of Variance, and Standard Deviation Index) should be performed.

## Acceptable Range

It is important for the blood bank to understand how the EQA acceptable ranges are set so that they can properly interpret their EQA report.

- The acceptable range is the analytical range around the central value and it is a tool for review of EQA results in both numerical and graphical report formats.
- A result outside the acceptable range should alert the blood bank that their assay may produce results that are at risk of detrimentally affecting decision making

Acceptable Range can be based on statistical comparison, regulatory requirements, clinical need, expert opinion and other criteria. Blood bank should be aware of the turn around time of EQA, time of receipt of samples, reports etc. It should be better to get them earlier as it is easy to remember what was happening in the blood bank and proper corrective action can be taken sooner. Organizing laboratory should add a comment on the performance if it is in the unacceptable range along with suggestions on improvement.

## Corrective Action

Blood bank should detect outliers and perform RCA with CAPA.

## Follow up of rules of EQA

- Participants' results should always be confidential
- Reports of deviation in results should be given only to the participants!  
Serious errors should be actively followed up eg.,
- Blood grouping (ABO Rh)
- Tests for infectious diseases (false negative results)
- Blood Bank management should monitor EQA results and implementation of corrective actions when control criteria are not fulfilled.

## Benefits of Participation in EQA

Benefit the participating laboratories:

- Identification of inaccuracies in test results of Blood Bank
- Guides Blood Bank in corrective action and improvement
- Raises awareness of the successes and challenges in Blood Bank practice
- Provides information for advocacy

EQA participation creates a network for communication, and can be a good tool for enhancing a national blood bank /laboratory network. Samples received for EQA testing, as well as the information shared by the EQA provider, are useful for conducting continuing education activities.



## CHAPTER 22

### Performance Improvement

Performance improvement is a method of assessment of procedures, activities, or human resources on certain parameters keeping the pre established criteria and objectives as a benchmark.

Benchmarking is a structured, continuous, collaborative process in which comparisons for selected indicators are used to identify factors, which when implemented will improve transfusion practices.

The goal of performance improvement is provision of high quality services. Results are achieved through a process that describes desired performance, identifies gaps between desired and actual performance, identifies root causes, selects interventions to close the gaps and measures changes in performance.

Performance monitoring is a proactive strategy, for quality assurance in blood bank

### Methods of Performance improvement

#### Strategy for quality management systems

1. BTS should establish a quality management system that includes organizational structure, responsibilities, policies, processes, procedures, and resources to achieve and maintain quality.
2. QMS should identify key personnel and define their responsibilities as Quality manager, asst. quality manager and designate responsible technicians who should all formally meet on a regular basis to monitor, support and work towards quality management.
3. Quality assurance activities should include development of documents such as standard operating procedures (SOPs) and training of personnel. They should also conduct reviews and analysis of operational performance data to determine the state of the overall process, to detect any deviation/adverse events.
4. BTS should develop a comprehensive programme of quality improvement which integrates patient, clinical and managerial approaches. It should specify the nature and purpose of clinical audit to be conducted by involvement of all doctors for clinical use of blood.
5. Blood bank should identify Critical Control Points and constantly monitor those to assure there is no laxity of services. The ultimate goal is to provide safe transfusion to the patients.
6. BTS should develop SOP with defined procedures for responding to adverse incidents, near misses, handling complaints, assessment of donor satisfaction. All members of staff should be trained to identify, assess, and report any outliers so that root cause analysis and appropriate actions could be taken timely.
7. BTS should impart regular annual training given to all hospital staff on topics such as "hemovigilance" to increase awareness regarding the reporting of adverse events related to blood transfusion

## **Continual Quality Improvement**

The ultimate goal of performance improvement is to enable BTS to attain higher levels of performance by creating new or better standards or removing the deficiencies in products, processes, or services for continual quality improvement.

Blood Bank should continually improve the effectiveness of QMS, including the pre-examination, examination and post-examination processes through Quality Indicators.

BTS action plans should be directed towards areas of highest priority based on risk assessments. The staff should be communicated about plans and related goals of quality improvement for their participation.

Performance monitoring by monitoring and analysis of quality indicators, Implementation of appropriate corrective measures for continuous product and service quality improvement.

### **Quality indicators(QI):**

Quality Indicators are important tools for quality management system to monitor and control efficiency of the key systems. Heightened efforts towards identifying, selecting, establishing and analyzing QI has urged attention towards defining QI in blood banks.

QI provide proof of the level of quality of performance and the information gained should be used to seek improvement in the quality of performance of blood bank.

QI are performance measures designed to monitor one or more processes during a defined time and are useful for evaluating service demands, production, personnel, inventory control, and process stability. Measure can be expressed e.g. as % defects (% outside specified requirements), defects per million occasions (DPMO) or on six-sigma scale. They are used by the regulatory and inspection authorities to provide information regarding the safety of the safety of blood bank processes for efficacious treatment of patients.

### **Objectives of Quality Indicators :**

- Insight into the level of quality in services and products
- Enable Management review on QMS conformity with the set standards and take corrective action on Deviations and any adverse events
- Enable professionals and organizations to monitor and evaluate
- Enable comparison of institutions of similar characteristics (benchmarking)
- Support patient choice of providers.
- Important for the process of accreditation and certification

### **Characteristics of QI:**

- Critical importance and have potential for use
- Reliable and valid
- Uniform and comprehensive data collection

- Monitored continuously for trends & detection of deviations
- Necessitate appropriate corrective and preventive measures

### Types of QI:

- Rate or mean based QI provide a quantitative basis for quality improvement. Proportion or rate-based indicators need both a numerator and a denominator specifying the population at risk for an event and the period of time over which the event may take place.
- Sentinel QI identify incidents that trigger further investigation. They represent the extreme of poor performance and are generally used for risk management.
- Generic QI express the quality of care

### Classification :

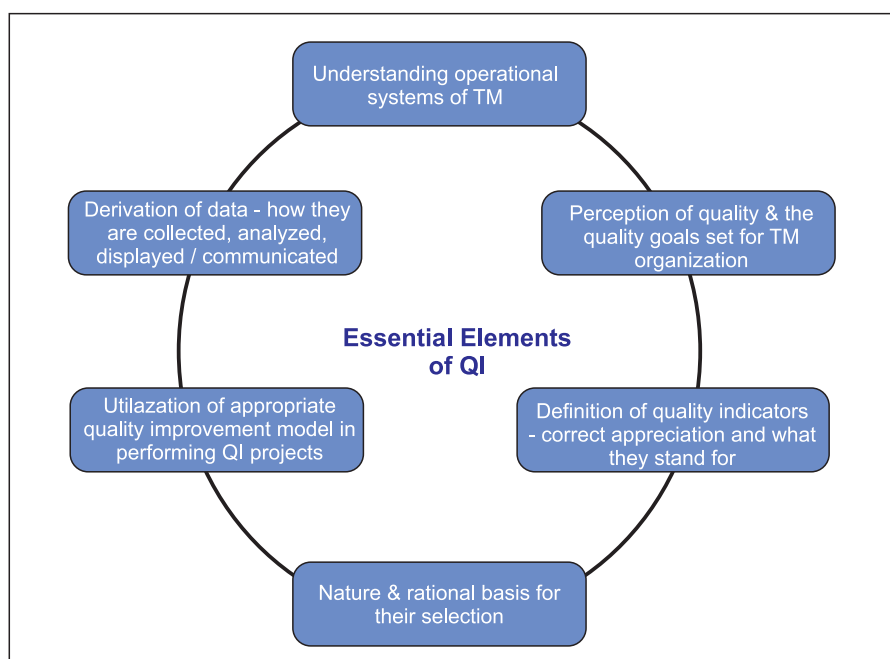
#### 1 In line with the tripartite quality model

- Structural indicators—how well the transfusion processes are organized in terms of status of manpower, equipment and materials required for processes in blood bank. Wrong or defective blood bag used in blood collection, components storage deficiencies due to faulty storage equipment are some of the examples of structural indicators.
- Process indicators—how well the activities are performed eg TAT
- Outcome indicators – how well appropriate results are achieved eg Discard rates, Expiry rates, Adverse events, CT ratio

#### 2 According to the objectives of their establishment and utilization

- Internal quality indicators defined by the institutional management.
- External quality indicators defined by external bodies to be used Nationally or Internationally as External Proficiency Testing or Accreditation Assessments

### Elements of QI :





The various stakeholders in the blood bank should monitor QI for improvement in their quality performance. Clinicians as well as BTS should ensure appropriate selection of quality indicators for effective analysis and efficient monitoring of quality.

Identification of the Critical Control Points (CCP) and Key Elements (KE) for blood bank operational system should be the fundamental pre-requisite for determining placements of quality indicators. Critical control points are those major processes of the operating systems that should function properly to obtain quality outcomes. KEs are operational steps that lead to CCPs. These KEs have to be effectively managed for the process to be free from errors. eg CCP and KE for blood collection, pretransfusion and administration of blood are as under.

| Operating Systems | Critical control points   | Quality indicators  |
|-------------------|---|---|
| Blood Collection  | Blood collection equipment and supplies set up<br>Donor re-identification | <ul style="list-style-type: none"> <li>• Wrong / defective blood containers</li> <li>• Donor identification failure</li> <li>• Rate of bacterial contamination of component due to poor arms cleansing</li> </ul> |
|                   | Donor phlebotomy  | Rate of donor phlebotomy failures   |
|                   | Post - donation events and care   | <ul style="list-style-type: none"> <li>• Labeling errors for donor unit and / or specimen</li> <li>• Adverse donor reaction</li> </ul>  |
|                   |   | Donor satisfaction survey   |
|                   |   | Elective surgeries deferment rate due to inventory shortage   |

| Operating Systems | Critical control points  | Quality indicators   |
|-------------------|--|--|
| Pre transfusion   | Ordering<br>Recipient positive<br>Identification                               | <ul style="list-style-type: none"> <li>• Wrong request / use of wrong request form</li> <li>• Incompletely filled request form</li> <li>• Non documentation of order/ consent / trigger for transfusion</li> </ul> |
|                   | Specimen collection and Labelling  | Discrepancy between specimen label & request form information  |
|                   | Request & specimen receipt   | Absence of identifying information on specimen / form  |
|                   | Recipient ABO/Rh, ABS, ABID, Tx, & difficult serological results records check | Request delivery TAT<br>Accessioning / clerical Errors   |
|                   | Donor / Recipient ABO / Rh, ABS, ABID testing                                  | Serological typing errors<br>Tests completion TAT  |
|                   | Blood component selection/ XM testing  | Component storage<br>Deficiencies  |

| Operating systems                     | Critical control points  | Quality indicators   |
|---------------------------------------|--|--|
| <b>Blood Component Administration</b> | <ul style="list-style-type: none"> <li>• Blood components release &amp; delivery for transfusion</li> <li>• Recipient pre-transfusion</li> <li>• bedside positive</li> <li>• Identification</li> </ul> | Component emergency release TAT  |
|                                       | Recipient transfusion & Monitoring   | Wrong component selection / release<br>Appropriateness of transfusion<br>Customer satisfaction   |
|                                       | Detecting, reporting & work -up of suspected adverse events  | Sentinel Events rates<br>Near-miss events rate   |
|                                       | Appropriateness of component request and use   | Component wastage rate<br>CT ratio   |
|                                       | Component disposition tracing  | <ul style="list-style-type: none"> <li>• Rate of inability to track disposition of component</li> <li>• Multiple donor exposure rates in infant transfusion</li> </ul> |

QI should address all activities within the blood bank but their number should not be too great in order to avoid administrative burden upon the workers. They should cover pre-analytical, analytical and post-analytical processes to the degree to which a set of inherent characteristics fulfills requirements (ISO 15189:2012)

The following quality indicators have been identified for BTS.

### Quality Indicators for Blood bank

|  |   |
|--|---|
| TTI%                                     | $\frac{\text{Combined TTI cases (HIV + HBV + HCV + Syphilis + MP)}}{\text{Total no. of donors}} \times 100$   |
| Adverse Transfusion Reaction Rate %      | $\frac{\text{No. of adverse transfusion reactions}}{\text{Total number of blood and component issues}} \times 100$  |
| Wastage Rates                            | $\frac{\text{No. of blood / blood component discarded}}{\text{Total no. of blood / blood components issued}} \times 100$  |
| Turnaround Time (TAT) of Blood Issues    | <p>Sum of the time taken<br/>Total number of blood and blood components cross matched / reserved<br/>(Time taken to be calculated from the time the request / sample is received in the blood bank till the blood is cross matched / reserved and available for transfusion. Blood bank shall set upper limits for routine and emergency issues separately)</p> |
| Adverse Donor Reaction Rate %            | $\frac{\text{No. of donors experiencing adverse reaction}}{\text{Total no. of donors}} \times 100$  |
| Component QC failures for each component | $\frac{\text{No. of component QC failures}}{\text{Total no. of component tested}} \times 100$   |
| Donor Deferral Rate                      | $\frac{\text{No. of donor deferrals}}{\text{Total no. of donation + total no. of deferrals}} \times 100$  |
| % of components                          | $\frac{\text{Total component issues}}{\text{Total whole blood + component issues}} \times 100$  |
| TTI outliers % age                       | No. of deviations beyond $\pm 2SD \times 100$   |
| Total no. of batch assays                | Delays in transfusion beyond 30 min after issue - sample audit vby BB every month   |

Additional quality indicators also may be adopted as :

1. Donor /clinician satisfaction
2. % of defective Blood Bags
3. Number of transcriptional errors/month
4. Number of patient complaints
5. EQA discordant results

### Bench Marks for QI

| 1 | % (Blood units discarded because of reactive/ TTI) / Total units collected in the given period | Bench - Marks  | Remarks                          |
|---|--|--|----------------------------------|
|   | TOTAL NO. OF DONATION  |  | As per Published data from India |
|   | HIV  | 0.28% HIV  |                                  |
|   | HBsAg  | 2-3% HBsAg   |                                  |
|   | HCV  | 0.4 - 2% HCV   |                                  |
|   | VDRL / TPHA  | 0.11% Syphilis   |                                  |
|   | NAT  |  |                                  |
|   | Malaria  | 0.03%Malaria   |                                  |
|   | Total  | Total < 4%   |                                  |
| 2 | Percentage of blood component usage 100% component preparation                                 |  | As per government recommendation |
|   | PRBC   | 100%   |                                  |
|   | FFP+CRYO   |  |                                  |
|   | RDP + SDP + PBSC +Buffy coat   |  |                                  |
| 3 | Adverse Transfusion Reaction Rate  | Hemolytic transfusiion reactions 0%  | As per Published Data            |
|   | Total Blood / Blood component issued   | Non hemolytic transfusion reactions  |                                  |
|   | % of transfusion Reaction  | <2%  |                                  |
| 4 | Wastage Rate   |  | As per Published Data            |
|   | Total no. of component Issued  |  |                                  |
|   | No.of unit received back for discarding  | <1%  |                                  |
| 5 | Percentage of wastage of blood and blood products( on shelf )                                  |  | As per Published Data            |
|   | PRBC   | <1%  |                                  |
|   | RDP +SDP   | <22% (As per indian Literature because of shelf life of platelets being 5 days only) |                                  |
|   | FFP + CRYO   | <1%  |                                  |

(cont...)

|    | % (Blood units discarded because of reactive/TTI) / Total units collected in the given period | Bench - Marks  | Remarks                |
|----|---|--|------------------------|
| 6  | Turnaround time for reserve of blood and blood components for patient<br>TAT                  | 120 minutes ( 45 minutes for Abtibody screening + 45 minutes for crossmatch + 20 minutes for blood grouping +10 minutes paper work ) | Selfset Parameter      |
| 7  | Turnaround time for issue of blood and blood components ( after receiving issue slip )        |  | Selfset Parameter      |
|    | PRBC  | (8 minutes for 1PRBC)  |                        |
|    | RDP+SDP   | (5 minutes for per unit)   |                        |
|    | FFP   | (35 minutes per unit and 60 minutes for 4 units)   |                        |
| 8  | Component QC Failure  |  | As per Govt Guidelines |
|    | PRBC, RDP, SDP, FFP, CRYO   |  |                        |
|    | Total no of test done   |  |                        |
|    | QC Failure  | 75% should conform to QC standards   |                        |
| 9  | Adverse Donor Reaction Rate   | <2%  | Self set parameter     |
| 10 | Donor Deferral Rate   |  |                        |
|    | Temporary / Permanent Deferral  | No set bench mark  |                        |
| 11 | Delays in transfusion beyond 30 min after issue   | <15%   | Self set parameter     |
| 12 | TTI Outliers % age<br>NO of deviations beyond + 2SD   | 0%   | Self set parameter     |

### Compilation of Data :

Data should either be compiled manually or electronically , Electronic data is an asset for storage, timely retrieval, analysis and display. Check Sheets are useful for collecting and analysing data particularly of observational and frequency.

Analysis of data should be done to elicit correct interpretations by Statistical tools as Histograms, Run / Control / Pie / Pareto charts, scatter plots, cause and effect diagrams, tests of significance as well as analysis of variance.

Any unexpected significant undesirable variation that constitutes sentinel event should be shared with national hemovigilance

### **Importance of monitoring and data Analysis of QI provides :**

1. Data on the incidence and prevalence of TTIs- important for safety of the donor pool
2. Trend analyses on donor reactions may reveal that reactions can be linked with
  - a. Age/Sex/Ethnicity of donor
  - b. Body weight of the donor
  - c. Phlebotomist
  - d. Procedure
  - e. Machines or devices
  - f. Temperature & Humidity in the donation room
  - g. Moment at which time the blood is donated etc.
3. Donor satisfaction level on the donation process using the number of complaints
  - a. Analyzing these on nature and frequency.
  - b. Indirectly affect the return rate of donors.
  - c. Post-donation process monitoring QI on recalls of units or specific blood components, the number and types of look-backs, haemovigilance notifications and near-misses at the production unit and the clinical units.

Different models particularly notable models used for CQI are-

- FOCUS-PDCA –relevant for TM
- Six-sigma
- The Lean & the Lean-Six-sigma

**FOCUS helps to focus attention at a discrete opportunity to improve**

PDCA phase allows for pursuit of the opportunity to improve and assessment of effectiveness or otherwise of the interventions applied.

| FOCUS   | PDCA   |
|---|--|
| F=Find what needs to be improved on                         | P=Plan for changes to cause improvement; PLAN brainstorming, flowcharting, evaluation using matrix, use of solution / fault tree   |
| O=Organize team with good knowledge in the process          | D=Do the changes initially small-scale as trial<br>DO' phase examples include - conflict resolution / leadership skill, training, experimental designing   |
| C = Clarify the present knowledge of the process            | C=Check to see if data indicate changes are effective; CHECK' phase are data-sheets, control charts, key performance indicators  |
| U=Understand factors responsible for variation              | A=Act consolidate gains made, implement change and strive to further improve process. ACT' are process delineation and standardization, training, reference standards, guidelines, benchmarks or thresholds are relevant |
| S=Select interventions that evidently might improve process |  |

Compilation and review of data by Quality Manager for the month should be finally shared with Management / I/C blood bank / Technical staff to ensure improvements based on data-driven analysis, ongoing measurement and assessment program fundamental to that process. The improvement in overall performance is a positive indicator.

**Root cause Analysis**

- Root-cause analysis (RCA) : Systematic, extensive and in-depth analysis of a problem with the view to elicit most basic reason (s) that give rise to the problem.
- Failure mode and effect analysis (FMEA): Early detection of defects, determination of cause(s) of the defects and the proactive elimination of the causes of the defects resulting in improved process and product.

**Training of personnel** - Essential for involvement of all staff as each and every process has an effect on the quality indicators. Training provides-

- Clarity in procedures
- Monitoring of each aspect of the process
- Observation of Trend analyses
- Regular and annual reporting of data - needed to capture this process and to understand where the changes should take place in order to improve the system.

Effective leadership and initiative are fundamental building blocks for establishing QIs. At institutional level, the leadership and initiative should be from the Institution's management. At National/International level, various quality-driven organizations often perform this role.

**(Please refer to Annexure - K)**





## CHAPTER 23

### Internal Audit

**Audit is a management tool for monitoring the quality assurance system.** It is a systematic and independent examination to determine whether quality activities are related and results comply with planned arrangements by the blood bank.

It is a process to confirm or negate that established, approved policies and SOPs are properly implemented. It investigates to obtain evidence and evaluates it objectively to determine the extent to which audit criteria are fulfilled. Audit procedure may be internal or external.

Internal audit is a well planned comprehensive audit that should cover each activity of a blood bank for technical compliance. It can however be a selective audit focusing on specific areas.

### Objective of Internal Audit

- To enable the Blood Bank to learn “where we are in terms of Quality Management, measure gaps , and provide information on further planning, monitoring and continuous improvement
- To verify that BB operations continue to comply with the requirements of the QMS (ISO 15189:2012).
- To provide evidence to demonstrate that the QMS has been effectively established, implemented and maintained.

### Procedure for Audit

Blood Bank should lay down policies and SOP's for internal audit. The procedure for internal audit should include an audit plan, frequency of audit, methodologies and requirements for documentation.

Audits should be formally planned and organized by Quality Manager and are carried out by a trained internal auditor independent of activity. The deficiencies of audit should be noted and results documented and reported to management for review and prompt action Appropriate corrective/ preventive action should be carried out within the agreed time frame.

**Audit planning** - Audit should be conducted as per Quality system procedure to fulfill all clauses of ISO15189 standards, scheduled and planned with prior information to the auditors within a time period required to complete the audit.

1. All departments should be covered at the same time to ensure coverage of all activities.
2. Audit should be carried by the personnel trained in audit ,techniques and processes of blood banks. Audit should not be conducted on own department.
3. Should ensure availability of auditors before hand and properly coordinate all activities.
4. Documents as Quality manual, Checklist, Formats etc should be kept ready.
5. Auditors ask questions, observe activities, examine facilities, examine records and conformity to of activities with standards.
6. Auditors should verify what is done and what is said or written and record observations with

evidence.

7. Auditors finally review and analyse observations and classify as Non conformities and deviations. If negative findings are found , more areas should be audited by them.
8. Define deviations as Major &/or Minor or deviation  
Major: Requirement of standards missing/not implemented directly affecting patient care  
Minor: All deviations excluding Major
9. A report sheet should be prepared by auditors to present both positive and negative findings for follow up and corrective actions
10. Interval between audit/ report/ close out--Follow up corrective action should be defined.

#### **Audit may be planned as Vertical or Horizontal Audit**

| <b>Vertical Audit</b>   | <b>Horizontal Audit</b>  |
|---|--|
| Selection of a single request form and its associated sample ( the input ) and following through every element of the process until the report is produced ( the output ) | Selection of one element of the process for example the TTI report and examine a no. of reports to see whether appropriate interpretation and / or follow up of abnormal results had been provided |

#### **Different Areas Covered in Audit are as follows:**

**Structure Audit : Audits the resources available as per ( Drug and Cosmetic Act 1945 with amendments ) in terms of**

- Man power: sufficient/shortage
- Materials and supplies
- Machines : functional/non functional

**Process Audit : Audits the procedures in the blood bank**

- Donor Recruitment/Selection
- Blood Collection
- Component Preparation
- Testing for Infection Markers
- Cross – matching /Antibody identification
- Issuance of Blood Component
- Discarding

**Quality Audit in terms of implementation of the QMS**

- Organizational structure
- Personnel job description

- Quality policy
- Management review
- Complaints/Feedback
- Inventory management

**Output Audit : Audit in terms of quality of services rendered:**

- Total no. of donors
- Total no. of units collected
- Total no. of components prepared
- Total no. of tests done
- Total no. of cross match
- Total no. of units issued
- Total no. of units transfused
- Total no. of units received back
- Voluntary/ Replacement donors

**Outcome Audit : Audit in term of health benefits to the patient:**

- Appropriate use of blood components
- Adverse transfusion reaction (Haemovigilance)

**Example**

The minimum criteria for form/ specimen acceptance in compliance with standards:

- Review non conforming specimen form issues for that day
- Review centrifugation, aliquoting, quality checks
- Review the test method including:-
  - Maintenance files on IT system
  - Review of results on the instrument
  - Release of results to patient's file
- QC performed prior to release of results
- EQA scheme in place for test
- Turnaround time
- Verify the Laboratory instrument is secure from uncontrolled access
  - Data on the LIS is backed up at defined intervals
  - Back up discs are labeled properly and stored securely
- Equipment file
  - Calibration records
  - User requirement specification
  - IQ, OQ data
- Environmental monitoring
- Perform audit trail on processing an urgent sample

### Checklist Horizontal Audit

|          |           |            |            |                |
|----------|-----------|------------|------------|----------------|
| CIRCULAR |           |            | Issue date |                |
|          |           |            |            |                |
|          | Internal  | Audit Time | Table      |                |
|          |           |            |            |                |
| Date     | Time      | Auditor    | Auditee    | Clause Nos     |
| 1/6/2012 | Morning   | Auditor 1  | 1          | Clause Nos 1-5 |
| 2/6/2012 | Afternoon | Auditor 2  | 2          | Clause No 6    |
| 3/6/2012 | Full day  | Auditor 3  | 3          | Clause No 7-11 |
|          |           |            |            |                |

Prepared by QM in consultation with HOD/TM

Signed by HOD/ TM

### Checklist Vertical Audit

#### MONTHLY VERTICAL AUDIT FOR TRACEABILITY OF BLOOD BAG

Month: \_\_\_\_\_

Donor ID/Blood Bag No.: \_\_\_\_\_

Date of Collection: \_\_\_\_\_

1. Donor form – Complete / Incomplete
2. Pre-donation testing acceptable – Yes / No
3. Type of bag used for collection – Single/Double/Triple/Quadruple/Penta
4. Name of phlebotomist and signature available – Yes / No
5. Name of Medical officer & signature available – Yes / No
6. Blood collection Date&time entered in donor form \_\_\_\_\_
7. Blood Components prepared Date & Time \_\_\_\_\_
8. Name of the components prepared: PRBC / RDP / FFP / CRYO / CPP / WB
9. Are all the Components labeled Correctly – Yes / No
10. ELISA Report Printouts available – Yes / No
11. Results of TTI Tests done on blood bag updated in
  - Blood Request form / System - Yes / No
  - Donor Screening(TTI)Register - Yes / No
  - Master Register - Yes / No
  - Apheresis Master Register - Yes / No
 (In case of SDP unit)
12. TTI Screening results of Blood Bag – Positive / Negative
13. If TTI Screening is Negative Bag issued to .....

(Cont...)

14 Issued to

|                                     |            |            |            |
|-------------------------------------|------------|------------|------------|
| Bag no & component                  | RCC / PRBC | RDP        | FFP        |
| Name & Hospital No.of the Recipient |            |            |            |
| Date & Time of issue                |            |            |            |
| Compatibility Results               | Compatible | Compatible | Compatible |
| Billing Done                        | Yes / No   | Yes / No   | Yes / No   |

15. Documentation

- Blood Request / Cross match form - Yes / No
- System updated - Yes / No
- Blood Issue Register - Yes / No
- Screening and Compatibility reports in HIS (Yes/No)
- Master Register Entry updated - Yes / No
- If not entered Person responsible given to \_\_\_\_\_

16. If TTI Screening Reports are Positive, has the blood been discarded - Yes/ No

17. Discarded blood records are available in

- Autoclave register (Yes/No)
- Discarding register (Yes/No)
- Master register (Yes/No)

18. Has any unit been returned - Yes / No

19. Has the returned unit been re-issued - Yes / No / Not applicable

20. If so to whom has it been re-issued - \_\_\_\_\_ / Not applicable

21. In case of TTIPositivedonors,have they been counseled - Yes / No / Not applicable

22. Is address telephone No., E-mail available in donor form for communication results - Yes / No

Name and signature of  
Donor Area Supervisor

Verified by  
Medical Officer Signature

**Documentation of Internal Audit**

- Reports of internal audit and follow up corrective action should presented and taken up for discussion in management review meeting
- The findings and action arising from management review of internal audit findings should recorded and decisions made as a result of review
- The management should ensures that action on internal audit report should be discharged with appropriate and agreed-upon-time.
- A good audit plan should create a picture of complete manufacturing operation, with an intent of identifying areas where improvement are needed in processes, equipment, personnel performance, facilities or procedures.
- Please use self assessment quality check list given in annexure - K

**(Please refer to Annexure - L)**



## CHAPTER 24

### Management Review

Management has a major role in confirming the completeness, relevance and effectiveness of quality management systems.

Top management and the key members of the blood bank should examine the performance of the quality system as a whole. Management review should be conducted according to predetermined schedule and procedure (QSP) with an objective to decide whether the system is delivering what is required. Management should be able to introduce necessary changes or improvements in the system. The meeting should agree on who will carry out each actions and the timescale of completion.

Management should constitute a Review Committee. The members of the committee should be:

- Quality manager
- Technical manager/supervisor
- BB In-charge
- Representation from senior level of management of the institution, where decisions on allocation of resources are made
- Other members of management as per specific requirements

**Schedule of Management Review** meeting the meeting should be held at least once every 12 months. Meetings should be held at shorter intervals when a quality management system is being established. Management review meetings should follow internal audit, so that the results of audit may be discussed during the meeting.

### Responsibility of Quality Manager

Quality manager should arrange the meeting and compile and communicate of the agenda to all the members with their acknowledgment.

Quality manager should also ensure that all relevant documents are available including staff suggestions, internal audit report, and performance and calibration records of equipment.

### Meeting Agenda should include

1. Quality matters arising from last management review meeting and a report from Quality manager confirming that all actions have been taken.
2. Report on any surveillance or assessments by the accreditation body.
3. Discussion of the results of all audits, both internal and external.
4. Review of the quality manual and decisions on any changes required
5. Performance in EQA exercise
6. Plans for future participation in EQA
7. In-house quality control checks.
8. Review of staff training and plans for the following year.



9. Adequacy of staff, equipment and other resources to maintain quality.
10. Future plans for staffing, equipment, premises etc
11. Agreement on action points and date of next meeting.
12. Reports from managerial and supervisory personnel.
13. Corrective and preventive actions.
14. Changes in the volume and type of work.
15. Blood donor and clinician's feedback.
16. Recommendations for improvement.

### **Minutes of the Meeting**

- The minutes of meeting should be captured and a list of action points prepared.
- The quality manager should be responsible for ensuring that all of the actions agreed at the review meeting are carried out.
- Responsibilities of the personnel carrying out corrective and preventive actions within a time frame should be fixed.
- The results of the meeting should feed into the blood bank quality planning system and should include the goals, objectives and the action plans for the coming year.

### **Sample copy of Minutes of MRM**

#### **XYZ Blood bank**

Date .....

#### **Minutes of Management Review Meeting**

The First Management Review meeting was held on\_\_\_\_\_. The meeting was presided over by the Director. The following members were present:

1. I/C blood bank
2. Quality Manager /Asst. Quality Managers –
- 3 Technical manager
- 4 Representative from Administration section