INTERNSHIP REPORT

at *Molbio Diagnostics Pvt. Ltd. , Verna,*

Goa

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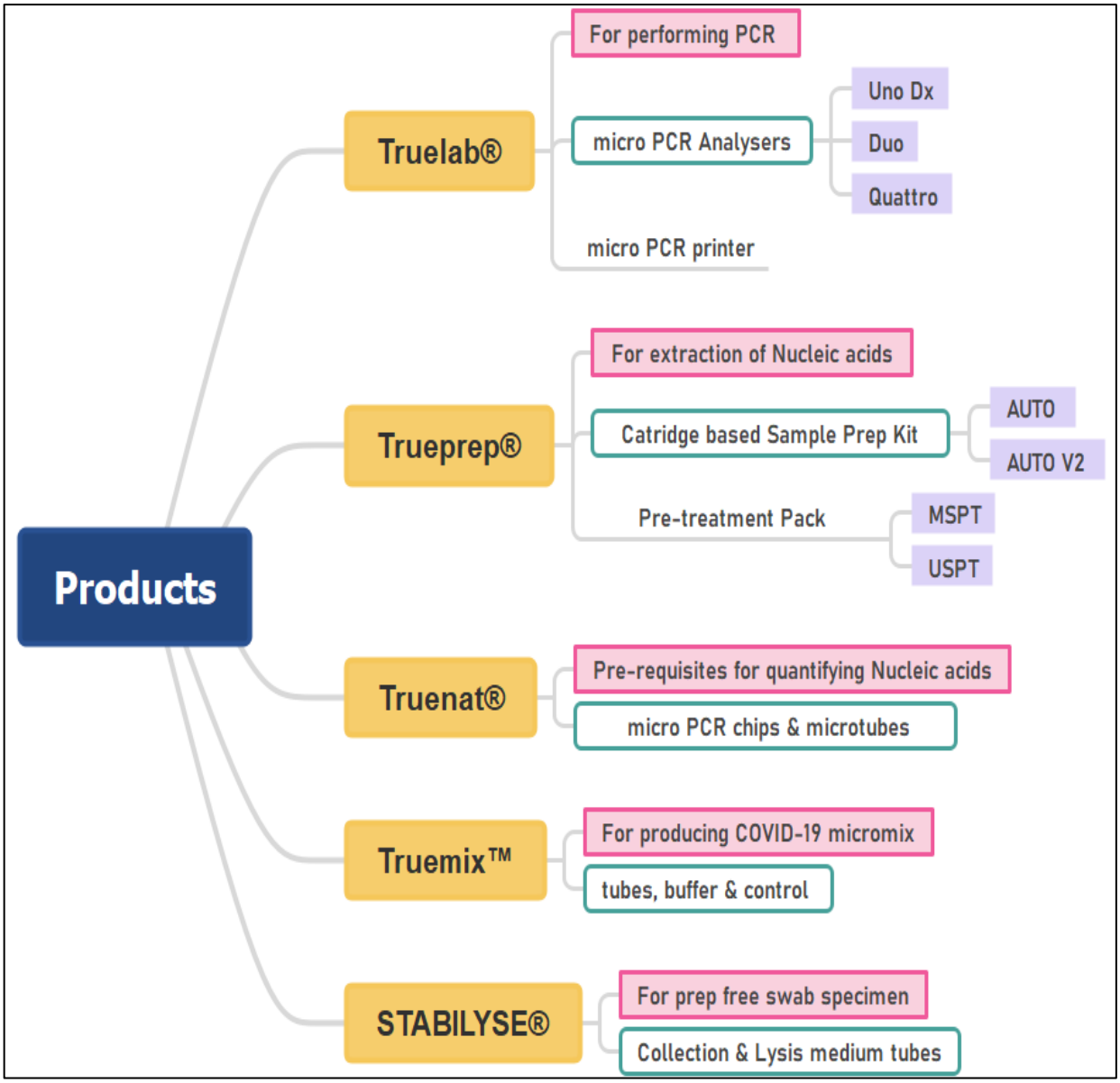
ABSTRACT

The present report briefly describes my internship experience at Molbio Diagnostics Pvt. Ltd., an in-vitro diagnostic medical equipment manufacturing company at Verna, Goa, from 1st to 31st December 2022. I had an opportunity to work as a Quality Assurance Intern among country's top 200 leading fronts in-vitro diagnostic companies. During this internship, I learnt the different duties performed by a QA officer, from arrival of raw materials till the dispatch of the final product. QA is divided into three departments; IPQA(In-Process Quality Assurance), QMS(Quality Management System) and RA(Regulatory Affairs). I worked in the IPQA and QMS department where I was assigned tasks like Log Book verification, Batch Review Checklist Verification for MTB, COVID-19,HIV and HBV, Verification of Stability Reports and Quality Testing, assisting in Lot pickup and Line Clearance. Through this internship, I acquired skills of verification and compliance of documents, giving line clearances and doing lot count, calibration of instrumentation, and critical analysis of Stability reports and Batch Review Checklist which is necessary prior to dispatching the final product.

INTRODUCTION

Molbio Diagnostics is an in-vitro diagnostic medical equipment manufacturing company, located in Verna, Goa. It was established in the year 2000, by Dr. Sriram Natarajan. with an intention of quick, precise and cost effective diagnosis of plethora of bacterial and viral diseases. This company manufactures five main types of products;

1. **Trueprep-** Fully automated AUTO Cartridges and AUTO V2 Cartridges that are disposable and used for the purification and extraction of nucleic acids from the clinical specimens.
2. **Truenat-** Disease- specific micro PCR chips used for obtaining results (CT values) from Quantitative real time PCR and are disposable ones.
3. **Truelab-** Quantitative Real Time micro PCR Analysers like Uno Dx ,Duo and Quattro 4x4.
4. **Truemix COVID-19** - a lyophilized, ready-to-use, duplex Real Time Reverse Transcription Polymerase Chain Reaction (RT PCR) test for the qualitative detection of SARS CoV-2 RNA in human oropharyngeal and nasopharyngeal swabs that aids in the diagnosis of COVID-19.
5. **STABILYSE** - a sample collection and lysis medium for oropharyngeal and nasopharyngeal swab specimens with a stability at temperature 2-40^{o}C for almost 2 years .



Products of MolBio Diagnostics Company

This company has marched its way to success at a steady pace right from developing India's first swine flu testing kit to being World's First Point-Of-Care Truelab Real Time Quantitative micro PCR system. This system is based on sample extraction and purification performed using a fully automated, cartridge-based Trueprep AUTO sample prep device, followed by loading the pure DNA in a disease specific Truenat microchip for Real Time PCR for quantifying and

diagnosing the disease. The most efficient use of this well -designed system was seen during the novel COVID-19 pandemic, where quick and accurate testing was need of the hour and diagnosis of the disease was much faster. Besides diagnosis, they also perform stability testing , which are of two types; real time stability and accelerated stability to ensure the long lasting duration of the kits.

MolBio Diagnostics Pvt Ltd. (Site I)

The major departments of the company are as follows :-

1. **Production**- It deals with production of the testing kits, TRUEPrep , TRUEmix and TRUENAT products.
2. **Quality Control-** It is a department that is responsible for maintaining the standards of manufactured products by testing a sample of the output against the specification.

3. **Quality Assurance**- It is a department to ensure that the products right from arrival of raw materials to the production of final kits is according to the standards, with no contaminants present and will meet quality requirements and all relevant regulations.
4. **Validation**- This department ensures that the instruments used in the production are calibrated, functioning properly and comply with the procedures/process/ method or activity to consistently produce the product to obtain the expected result (predetermined requirements)
5. **Marketing and Sales**- This department designs various strategies in offline and digital mode to attract the patients and raise awareness about the diagnostic testing kits . It is also responsible for identifying the target consumers like healthcare professionals.

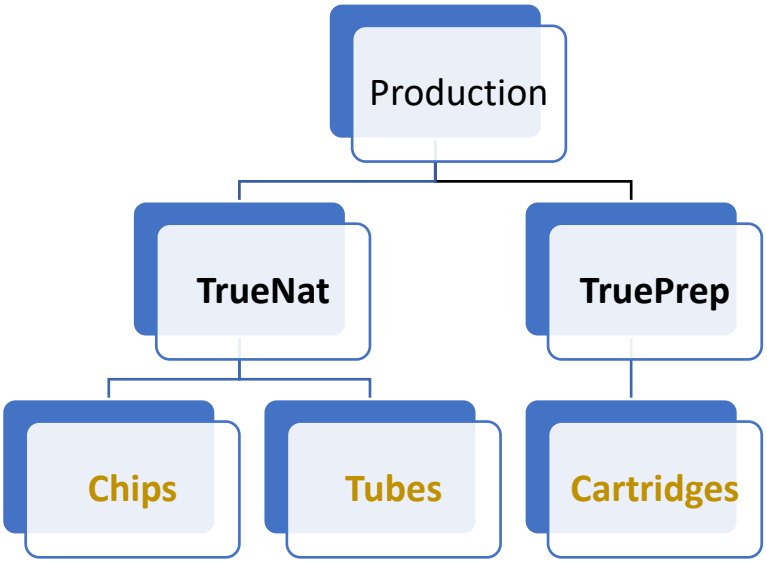
OBJECTIVES

The objectives of the present internship are as follows:-

- To understand the production and processing of a medical equipment manufacturing company.
- To know the basic setup and embankment of a diagnostic company.
- To acquire various skills as a Quality Assurance intern.

PRODUCTION

The production section comprises of 2 main products:-

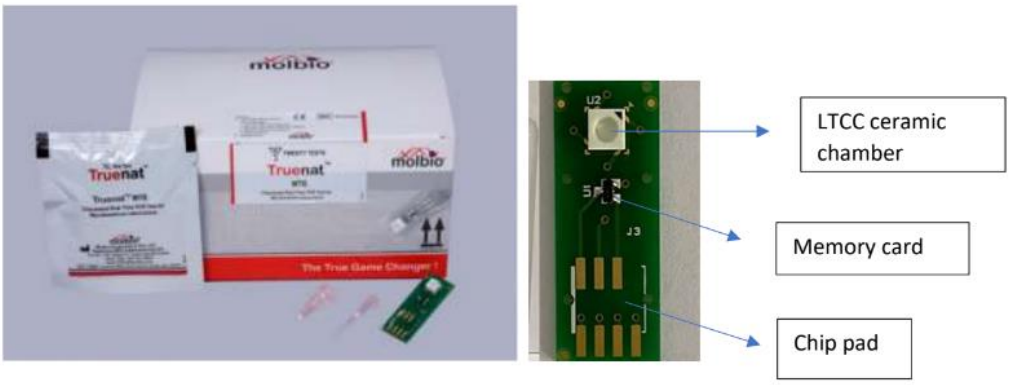


As mentioned earlier, I was interning at MolBio site 1 where TrueNat production was ongoing while Trueprep production was halted for time being. Hence, I was given a brief induction on TrueNat Production by respective departments. In addition to showing us the working of every machine and process, we simultaneously learnt the role and duties of Quality Assurance which occurs at every step. This made us realise the importance of the department we would be working under.

Given below is the production flow of TrueNat which occurs in a very efficient and systematic manner, along with the role of QA at every step :-

1. **Chip Sorting & Arrangement**

- Micro-chips are one of the most important components of the entire diagnostic process. They are disease specific and help in diagnosis of each disease.



Truenat® kit

- It comprises of 3 different parts ; memory card, LTCC chamber and chip pad.
- Upon arrival of the chips from the vendors, they are sent to QC for quality testing, if the required standard is met, they attach a Green Label to assure that the chips are "QC Approved".
- After the approval of QC, they are manually sorted according to their criteria and arranged in the trays stacked together ready for washing.
- *Role of QA:* At this stage , sometimes the QA is in charge of a duty termed as "lot pickup", whereby QA has to randomly open a packet with different lots of chip numbers and send them for QC testing.

- It is important to note that every count of the chips being used needs to be kept so that the final number is equal to the quantity purchased. For e.g., if QA picks up 50 Lots to be sampled and QC tests 100 Chip lots, then this number needs to be mentioned in a document for Incoming Raw Material, chemical or process. Once again after the completion of this process the QA department needs to check if the entries made in the document are correct and if the quantity used is matching.

2. **Chip Washing**

- Now the stacked trays of chips are washed thoroughly for cleaning purpose using UP(Ultrapure) water and EDI(Electrodeionised) water through a water system termed as Rephile Lab Water Purification system.
- The chips are washed twice in R-EDI and once in R-UP water.
- Microtubes and bungs are also purchased from the vendors and given for washing through the above mentioned process.

3. **Chip Oven Drying**

- Now, a random quantity of washed chips are once again sorted manually to see if they have undergone any damage and whether they are cleaned up to the standard. If yes, they are subjected to 20 minutes at 80C for oven drying to remove the moisture, followed by 20 mins of subjecting to UV treatment to disinfect the chips.

4. **Biomix Preparation**

- Biomix refers to the mixture of all the ingredients needed for the enzymatic reaction of PCR to take place. It is made in the form of a cake placed in the chip in such a way that when the contents of the sample are added in this cake, it gets inverted and the enzymatic reaction occurs smoothly within that chamber. Thus, proper formation of biomix cake is extremely important. To make this, there are two coats needed

  1. Bovine Serum Albumin(BSA) coat – 10uL.
  2. Hydrophilic Coat- 6uL

  (Depending on the performance of the product there are 3 further types, Hydrophilic coat, Low Glyerol Hydrophilic coat and moderate Glycerol hydrophilic coat. All the coats differ in Glyerol content but comprise of different compositions of 50mM $MgCl_2$, 40% Trehalose, 10% Tween and remaining is filled with Double Distilled water).

- *Role of QA:* At this stage , QA officer must be present at the time of dispensing the coat and performing a duty called "Line Clearance". Line Clearance refers to giving a clearance for the required process to start or continue in process or for a particular material to be approved, by the QA , if it meets the required standard. Here, QA officer must ensure all the instruments are calibrated, temperature sheets are maintained and the temperature sheet is filled completely. All the materials required for bio mix dispensing are present and the remaining materials must be kept aside.

The QA officer will check if all the requirements are up to date, of good quality and then sign the document, thus Approving Line clearance. Once line is cleared, the production officers may proceed to coat the chip with biomix. Without the line clearance by QA, this process wont initiate and can be halted at any time if QA officer feels certain components are missing , not up to date or back dated.

5. **Chip Dispsensing**

- Chips are cleaned using isopropyl alcohol(IPA). The silver lining of the chip is blow dried and using the Reagent dispensing machine, the Biomix coat is dispensed at a fast speed using Jet system. In one tray , around 240 chips are dispensed. Then, a random group of chips (2 chips/tray) are manually checked for dispensing to see if 10uL exactly fits the chip well. Now these chips are placed in the cabinet in the VDT for drying at 670-720 vaccum for 1 hour.
- Chips are now dispensed with 5.8-6.2 mg wax /polymer using the biodot wax dispensing machine. However, prior to wax dispensing it needs to be filtered, melted(40C) , weighed, measured for moisture content(<3.5), jet pressure and fluid pressure.
- *Role of QA:* At this stage , QA officer must be present at the time of dispensing the coat for giving "Line Clearance".

6. **Flash writing**

- Once the chips are dispensed with wax , they are subjected to a process called flash writing. This is done using functional tester with conveyor belt where the chips are attached with pogo pins. This makes the chips specific to a given disease and once the process is completed, they are manually checked. If the flashed chips are within the given resistance and temperature range, then it is given a green pass(approved).

7. <u>Mastermix Preparation</u>

- As mentioned earlier, the TrueNat section also comprises of tube preparation. These tubes along with bungs and purchased from the vendors, washed thoroughly and subjected to disinfection. They are loaded with a component called Mastermix. Mastermix includes all the recipe like enzymes, primers, probes, buffer with the exception of the sample. This mixture is light sensitive and hence needs to be dispensed in the dark and done quickly. The primers are usually in lyophilised form (solid) with TE buffer and aliquots of different sizes are made. To check the mastermix , it is sent in vials of 3 and tested using PAGE and UV Spectrophotometry to check if the coating remains intact. This task is performed by QC. If there is no contamination and the cake is intact, then the mastermix is taken for performance testing to check the disease - specificity of the probe. Usually the vendors provide a highly concentrated probe which is diluted as per the requirement of the

mastermix content(dilution is usually 100uL) with 5-5.8V range. Now the Batch No. and AR No. is allotted and 6uL mastermix is dispensed in liquid state in the tube.

- *Role of QA:* At this stage , QA officer must check if the Batch No, Lot No. and the dilution of mastermix is as per the requirement.

8. Lyophilisation

- Once the tubes are coated with mastermix, they need to undergo a process known as lyophilisation (freezing and drying). This is done in a lyo machine which needs to be pre-cooled for 3 hours and needs to have a constant Air line of 6 Bar and Nitrogen Pressure of 0.2Bar. One lyo machine has 280 blocks, where trays are stacked after pre-cooling for freezing . 1 strip of mastermix coated and lyophilised tubes having the respective Lot No. are sent to QC for testing.
- Versafill dispensing machine is a device which is used for loading around 10K samples by a repetitive cyclic process of cleaning , priming(8ml) ,dispensing(6ul) and cleaning. Initially a certain amount of batch is taken for QC testing , knobs are adjusted accordingly so that the required amount is dispensed and primed . The block is checked and is followed by fast manual pipetting which is done in the presence of QA officer. Now the cool chain and lyophilised tray is brought from -20C and tubes are checked manually to see the mastermix is dispensed right at the bottom.

If not, the tubes are microcentrifuged for 2 seconds for the mastermix to settle down. Now the tubes are finally capped with bungs, but it is ensured that bungs are not pressed too hard as it needs to be completely vacuum. The temperature of probes should always be kept similar (-46C) and should dry at 42 hours.

- *Role of QA:* At this stage , QA officer is supposed to perform duty of "Line Clearance" for dispensing mastermix.

9. Pouching

- Once the chips are flash written and the tubes are prepared , they are stacked up for pouching which refers to a pouch comprising of all necessary equipments for nucleic acid estimation. It comprises of

a. Sleeve

b. Mastermix tube

c. Disease -specific chip

d. Micropipette tip

e. Activated silica

Truenat Kit

The 3 activated silica is used to drain out excess moisture. One shelf bag is double sealed , the seal is tested using dye leak test. This is done by QC. Finally the packaging occurs as pouches of same size or cartons of different size capacity 5T, 20T, 25T and 50T, with specifications of AR No. Lot No. are used. They are finally weighed and 1 carton and 2 pouches are sent for QC testing and approved by QA subsequently.

- *Role of QA:* At this stage , QA officer is supposed to perform duty of "Line Clearance" for pouching and Verification of all the documents.

QA DEPARTMENT

QA refers to “Quality Assurance” which means assuring that the quality of the final product and the process behind manufacturing the product is up to the standards, with no contamination and optimum use and is ready to be sold in the market. It is considered to be one of the most important departments in any pharmaceutical or manufacturing industry. This department ensures that at every step of the manufacturing process, the product is maintained upto a particular standard and once it is of the appropriate caliber, it gives line clearance of a particular product. Without the clearance given by QA, no process in the company can be initiated, no raw material can be used and no product can be sold, hence it is of prime importance. It is responsible for verification and compliance of each and every process performed, equipment used, testing of the raw materials that arrive, ensuring the products that are tested by “Quality Control” are of the required standard and then proceeding to approve it . Contrary to the popular belief that QA deals with “ Documentation” , this department has a much bigger role to play in the industry.

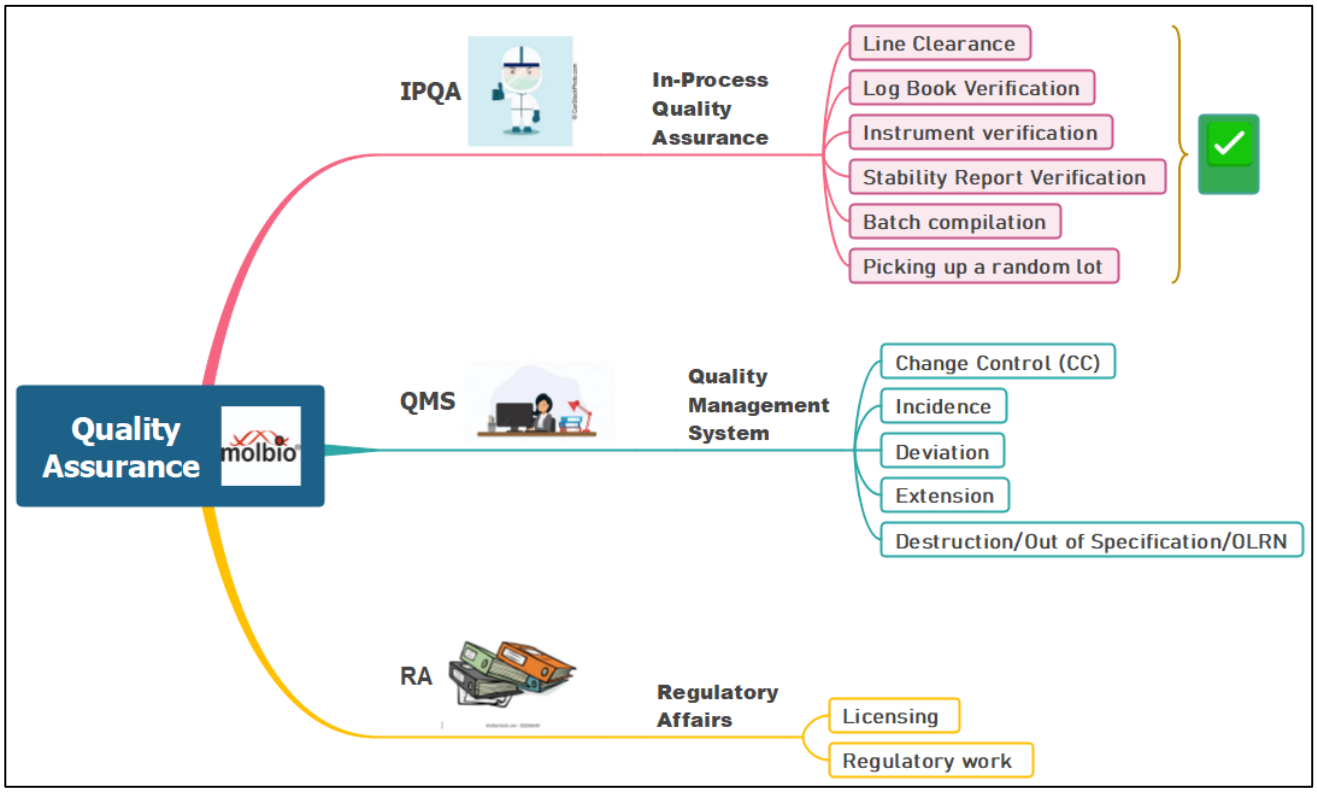
The role of Quality Assurance officer is extremely crucial and it begins right from the start of the production until dispatch of the testing kit. He /she in the quality assurance sector deals with compliance duties and verification at each and every task performed by other sectors of the company. Hence, he / she must know the standard testing protocols (STP) of each sub department.

The QA Sector is divided into three departments;

I. **IPQA(In-Process Quality Assurance)-** which executes duties performed during the production and processing.

II. **QMS(Quality Management System**) - that deals with any change in the processing like change control(CC), filing and verifying incidences, destruction, online rejection number(OLRN)

III. **RA(Regulatory Affairs)-** that deals with issuing licensing.



Sub-departments of QA

Inorder to understand the utmost importance of QA department, it is necessary to know the duties performed by the QA official. The different duties performed by QA department are as follows.

DUTIES OF QUALITY ASSURANCE DEPARTMENT

Given below are some of the most eminent duties performed by QA officers:-

- ✓ Giving line clearance for each activity right from arrival of raw material, chip sorting , polymer dispensing , master mix preparation, assembling of pouches to dispatch.
- ✓ Authorisation and Verification of logbooks of each instrument, equipment and activity from each department. Log books are maintained for each activity where the start and end time of the use of machine is noted, cleaning and use record is mentioned, is done and checked by the head of the respective department. This gives an idea about the usage of each device in the production section which needs to be verified twice a month within a span of 15 days by IPQA officer.
- ✓ The Activity Board is present in each Department , which mentions the Date , Time , Temperature, Lot No. Calibration status and what activity is to be conducted. The details of this activity board needs to be verified by IPQA especially while giving line clearance.
- ✓ A monthly data sheet of the temperature is maintained in each department as molecular diagnosis is temperature sensitive and it is absolutely necessary to maintain the same. It may differ depending on the equipment used but the temperature data sheet needs to be cross checked by QA and ensured that it is filled completely and up to date.

- ✓ A Transfer Note refers to movement of the particular chips or tubes or any device from one section to the other, which needs to be approved by the QA.
- ✓ Verification of Stability check to ensure longitivity of the product or time period of use.
- ✓ Issuing Online Rejection Note (OLRN) and approval of destruction forms. In case, there are instances where a particular batch of chips or tubes are faulty and needs to be rejected, prior to the commencement of this activity the given department needs to issue an OLRN and alert the QMS about it. In case, the batch is irreplaceable and needs to be destroyed then they need to file a destruction form. Incase of any deviation from a particular standard protocol, the QMS needs to be made aware about it and need their approval so that they can revise to STP.If a given process is not complete within the given time span, one can extend the time period by filing a extension form which needs to be coordinated by QMS.
- ✓ Monitoring the A.R approved products from QC.
- ✓ The most taxing and time consuming duty of QA officer is Batch compilation by filling up the details provided in the batch review checklist prior to dispatching.
- ✓ Performing an on site visit at certain departments like mastermix loading , chip dispatch etc.

- ✓ Checking the calibration of each instrument, temperature and Activity board during on site visit in various sub departments.
- ✓ Reviewing and issuing ***incidents, change control , deviation, extension and Master SOP.***

BRIEF OVERVIEW OF WORK CONDUCTED

About the company: Molbio Diagnostics is an in- vitro diagnosis medical equipment manufacturing company which produces testing kits for a plethora of diseases like malaria, dengue, TB and most recently, COVID -19. On our first day, we were briefed up about Molbio Diagnostics company. There are 6 sites of the company in India, two of which are located in Goa. They are termed as "site I " and "site V". My internship commenced on 1st December 2022 at site I. This site is preferably the first site where Molbio Diagnostics started. Currently, the production of stocks in this site is on halt. I was placed in the Quality Assurance sector of site 1. Dr. Sivakumar Selvaraj is the Quality Assurance Manager. On the first day of my internship, I was briefed about Quality Assurance and the variety of eminent roles played by Quality Assurance officer.

- The internship was conducted in the whole month of December 2022, with rigorous training at the start followed by performing certain basic tasks performed at the QA section of the company.

- As I commenced my internship in the QA sector at site I , I had a through induction on the various duties conducted by QA official.
- As a quality assurance intern, we were given brief introduction about the set of rules and regulations to be followed, the basic flow of manufacturing and the critical duties executed by quality assurance department.
- I have had an opportunity to work in the IPQA and QMS section where I was assigned tasks like Log Book verification, Batch Review Checklist Verification for MTB, COVID-19,HIV, HBV and many more diseases, Types of Stability Report Verification, Quality Testing Reports, Lot number and assisting Line Clearance.
- I , along with my colleague have compiled and cleared 131 Batches of MTB, COVID-19,HIV, HBV and H1N1disease.
- I have verified atleast 200 log books twice a month in the Production sector, IPC, QC sector, Dispatch sector and PCR sector.
- I have verified 100 Real-Time Stability reports and Accelerated Stability reports for MTB, Covid-19 and HBV.
- I have verified almost 50 Quality Testing Reports of QC.
- I have executed the duty of Lot number pickup (350 bungs).
- I have assisted in two Line Clearance duties; of mastermix dispensing and reintroducing MRP on the cartons of non exports.

- Unlike other sectors of the company who's role is limited to their specific department, the role of QA is important at every step from production to dispatch and customer's feedback. As such the duties of a QA officer extend to numerous ones such as giving line clearances for approval of raw materials , dispensing mastermix, dispatch of final product, selecting raw materials for QC testing and then approving the raw materials, verifying each and every instrument and equipment in use is calibrated and functional, verification of log books for each sector/instrument/process, filing incidences, approving change control in the Standard Operating Procedures(SOPs), approving deviation in any process or product, formulating Master SOP and CAPA(Corrective and Preventive Action). QA is responsible for any faulty product or complaint received by the customer or medical company.
- As a Quality Assurance intern, we acquired skills such as compiling batches, planning, executive skills, verification of documents, time management and compliance.

CONCLUSION

This internship served as a steppingstone to my venture in the pharmaceutical industry. As a new intern in the Quality Assurance Department, I was exposed to a plethora of verification and compliance work conducted by QA officers. I acquired the skills of compiling batches, log book verification, giving line clearances and filing incidences and keeping records of all the eminent documents. Thus efficiency, precision and being firm on your decision is crucial aspect of QA officer. Being at this post, one has to be critical and have knowledge about each and every aspect right from production to dispatch . In case, of any incidence or any fault in the final product, QA must be efficient enough to backtrace and realise where the mistake occurred and thus must be a keen observer.