INTERNSHIP REPORT

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INTRODUCTION

Molbio Diagnostics Private Limited is a non-governmental company, incorporated on 20th October 2000. It is majorly in manufacturing (Machinery and Equipment) business from last 22 years and currently company operations are active.

It is a Medical Equipment Manufacturing unit located at Verna Industrial Estate. Goa. Its main aim is to enable better medicine through precise, faster, cost effective diagnosis at the Point of Care (POC), to reduce patient suffering, fatalities and resultant economic loss due to inadequate diagnosis, to provide every patient access to best health care through cutting edge technologies and to stay connected to the needs of the patient through constant engagement with all stakeholders. Molbio offers a platform that can perform Molecular Diagnostics for infectious diseases such as HIV, HAV, HBV, Covid-19, MTB etc at the point-of-care on the Truelab Real Time Quantitative micro–PCR System.

Molbio has a clear vision to transform healthcare practices by providing near-care diagnostic solutions using robust portable platforms, to enable decentralisation and democratisation of diagnostics through high ended point of care technologies, to be a leading global player in the point of care diagnostics segment and to continue to innovate and bring new technologies for social betterment.

Their motto is IC3, which can be elaborated as- **I**ndependent Care- Diagnostics independent of extensive lab Infrastructure. **C**ontinuous Care- Diagnose and Treat on the first visit. Monitor treatment outcome. **C**ost Effective Care- Gold standard testing at affordable level. **C**onnected Care-Identify disease Hotspots. Identify new needs. Provide solutions.

The Research and Development Wing of Molbio Diagnostics Pvt. Ltd is located at Bigtec Labs in Bangalore India. Bigtec has developed various tests and nucleic acid preparation devices to facilitate "sample to result" molecular diagnostics in resource limited settings. The micro-PCR system has since been launched in India through the parent company, Molbio Diagnostics which has manufacturing and marketing base in Goa, India.

The internship was conducted from 1st December to 31st December and we were placed in different departments which included Quality Control, Quality Assurance and Validation. The main goal of undergoing an internship at Molbio Diagnostics was to get an insight on how it conducts various diagnostic and confirmatory tests, the equipment's used for conduction of these tests, the protocols and procedures followed and also to expand our knowledge on the various diseases prevalent in our society today and what are the kinds of tools used to diagnose these diseases.

I along with one of my batchmate were assigned to the Quality Assurance department. The Quality Assurance department mainly aims to assure the quality of products produced in the unit following the standard testing procedures and the standard operating procedures.

Products

1. Truelab®

Truelab® Uno Dx Real Time Quantitative micro–PCR Analyzer

Fully automated Real time Quantitative micro-PCR analyser, three wavelength system, performs between 10-12 test in 8 hours, controls amplification, detection and reporting of results.

Truelab® Duo Real Time Quantitative micro–PCR Analyzer

Fully automated Dual time quantitative micro-PCR analyser, two channel- Three wavelength system, perform 20- 24 test in 8 hours.

Truelab® Quattro Real Time Quantitative micro–PCR Analyzer

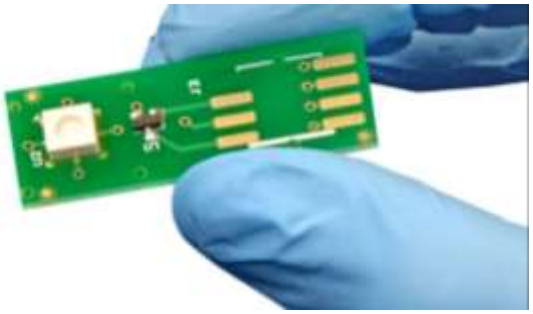
Fully automatic Real time Quantitative micro-PCR analyser, four channel-three wavelength system, performs 40-48 tests in 8 hours.

Truelab® micro–PCR Printer

Bluetooth Printer, prints wirelessly the results of the PCR tests performed by Truelab Uno Dx/Duo/Quattro Real Time Quantitative micro–PCR Analyzer

2. Truenat®

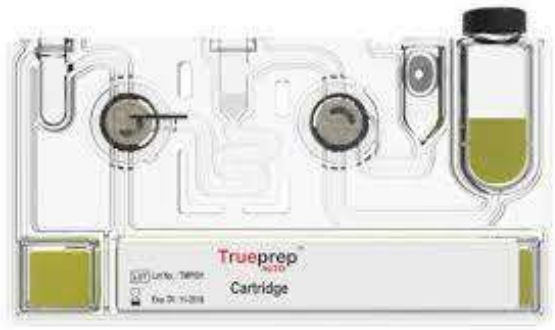
Truenat® Chip



Disease specific, ready-to-use and disposable micro-PCR chips that run on the Truelab Uno Dx/ Duo/Quattro to get quantitative real time PCR results.

3. Trueprep®

Trueprep® AUTO Cartridge



Disposable plastic cartridge for automated extraction of nucleic acids from clinical specimens.

Trueprep® AUTO Universal Cartridge Based Sample Prep Kit

Trueprep AUTO Universal Cartridge Based Sample Prep Kit works with Trueprep AUTO Universal Cartridge Based Sample Prep Device and is used for extraction and purification of nucleic acids from a wide range of biological specimens.

Contents of the Kit

A. The Reagent Pack contains the following reagents:

1. Wash Buffer A

2. Wash Buffer B

3. Elution Buffer

4. Priming Waste

B. The Cartridge Pack contains the following:

1. Cartridge

2. Elute collection tube

3. Elute collection tube label

4. Disposable Transfer Pipette-1ml

C. Disposable Transfer Pipettes (graduated) - 3 ml

D. Package Insert

Trueprep® AUTO v2 Universal Cartridge Based Sample Prep Device

Fully automatic sample prep device works in tandem with Trueprep AUTO cartridge and Trueprep AUTO v2 Reagent Kits for extraction and purification of nucleic acids from clinical specimen.

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2. Elute collection tube

3. Elute collection tube label

4. Disposable transfer pipette

C. Disposable Transfer Pipettes (graduated) - 3 ml

D. Reagent Reset Card

E. Package Insert

Trueprep® AUTO MTB Sample Pre-treatment Pack

It is used to liquefy and pre-treat the pulmonary and EPTB specimen before proceeding for extraction and purification of nucleic acids using Trueprep AUTO Universal Cartridge Based Sample Prep Kit and Trueprep AUTO Universal Cartridge Based Sample Prep Device.

Contents of the Kit

A. Liquefaction buffer

B. Lysis buffer

C. Disposable transfer pipette (graduated) - 1ml

D. Package Insert

Trueprep® AUTO Universal Sample Pre-treatment Pack

It is used to pre-treat the samples such as whole blood/ serum/ plasma/ urine/stool/swab specimen before proceeding for extraction and purification of nucleic acids using Trueprep AUTO Universal Cartridge Based Sample Prep Kit and Trueprep AUTO Universal Cartridge Based Sample Prep Device. Sample Pre-treatment decontaminates the specimen and makes it ready for storage/ transportation/ extraction.

Contents of the Kit

A. Lysis buffer

B. Disposable transfer pipette (graduated)

C. Pack insert

Trueprep® AUTO Transport Medium for Swab Specimen Pack

It is intended for use with clinician-collected endocervical, vaginal, anorectal, nasal and throat swab specimens. The transport media is used as a medium for collection, decontamination and transport of various types of swabs specimens before proceeding for pre-treatment using Lysis buffer, extraction and purification of nucleic acids using Trueprep Universal Cartridge Based Sample Prep Kit and Trueprep Universal Cartridge

Based Sample Prep Device. The transport medium will keep the nucleic acids of the respective organism intact thus maintaining the integrity of the nucleic acids. The medium does not maintain the viability of the microorganism. The collection and transport medium ensures for the safe collection and transport of the microorganisms which includes bacteria and viruses from the site of collection to the testing centre.

Contents of the Kit

A. Transport Medium for Swab specimen tubes (contains transport medium)

B. Pack insert

4. Truemix™

Truemix™ COVID -19

A lyophilized, ready-to-use, open format, 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 and aids in the diagnosis of COVID-19. The test detects the E and Orf1a genes of the virus. Truemix COVID-19 runs on standard Real Time PCR analysers.

Contents of the Kit

a. Lyophilized Truemix COVID-19 tubes

b. Reconstitution Buffer

c. Positive Control (Dried Down)

d. Negative Control

e. Strip of 8 PCR Flat Caps

f. Package Insert

5. STABILYSE®

STABILYSE® Prep Free

Sample collection and lysis medium for oropharyngeal and nasopharyngeal swab specimens.

Contents of the Kit

A. Collection and Lysis Medium Tubes

B. Pack insert

Major Departments and their Roles

I. Human Resource

HR department is a group who is responsible for managing the employee life cycle like recruiting, hiring, onboarding, training and firing employee and administering employee benefits,

II. Information Technology

IT department is responsible for hardware, software and networking of computers in the company. They ensure full access of employee to computer systems.

III. Validation

They validate process, products and machines. They ensure that the products meet's the standard.

IV. Manufacturing

They deal with manufacturing of the products. From washing- coat dispensing- wax dispensing- flash writing- pouching- packaging- dispatch.

V. Quality Control

Analysing and measuring. Conducting test, monitoring the production phase and checking the quality of all raw materials and products at every stage of production.

VI. Quality Assurance

This department is responsible for ensuring the products and the service meet the established standard set by the company and regulatory bodies.

VII. Marketing and Sales

It has responsibility for deciding where the company should sell and what its prices should be and includes choosing wholesale distributors or retailors.

Quality Assurance duties

QA is divided into IPQA (In Process Quality Assurance), QMS (Quality Management System) and Regulatory affairs.

QA officer- A person who deals with compliance and verification.

1. **Batch Compilation**

   QA compiles and verify the document of each lot of products manufactured. This include MSPT, USPT, etc.

   MSPT- used for MTB samples wherein sputum sample is collected which is very thick and hence viscosity has to be reduced using liquification buffer.

   USPT- used for samples other than sputum. E.g., blood, swab, etc. therefore liquification buffer is not used, it starts from preparation of lysis buffer.

   ATM- Auto Transport Medium

   Transport medium is used as medium for collection, decontamination and transport of various type of swab specimens before proceeding for pre-treatment using lysis buffer, extraction purification of nucleic acid using trueprep kit. Collection and transport medicine ensure for safe collection and transport of microorganisms which include bacteria and virus from site of collection.

   USPK- Trueprep Auto Universal Sample Pre-treatment pack. Version 1.0 and 1.5, buffers are filled in bottles, no connector tubes, bottles are received separately, and reagent reset card does not read in Auto device.

   VUCPK- Trueprep Auto V2 Universal Cartridge base sample prep kit. Version 2.0, buffers are filled in pouches, connectors are found, user friendly and reagent reset card reading.

2. **Issuing Documents**

   Document: Form of information that provides guidance or direction to perform a work, make a decision or provide a judgment. Document may also be template intended for recording data or result. Various documents needed by any department are issued by the QA department by the respective QA personnel. The needed documents are ordered by the concerned department via an inter-co, that has the details of the type of document and the number of copies required. The documents are issued by checking the document with pre-formed document,

document number, and number of copies and is followed with a signature and date on each and every page of the document of a QA personnel.

3. Record Room control

Records: special type of documents stating results achieved or providing evidence of activities performed.

Record Room: is a place where documents are archived. Document archive: process of placing documents in storage that needs to be kept but are no longer in use regularly.

Entry and exit in record room: Entry in record room is only allowed to authorize people, that includes QA personnel and certain department heads. (List of which is displayed outside the record room). Any other person entering the record room shall seek permission from the QA personnel and shall fill in the details of the individual along with the reason for entry. QA personnel accompanies the individual in the record room. Archival of documents is site specific and the archival be by the

Receiving and archiving Documents: user department to the QA via an inter-co or email. The documents received by the QA department is verified with the details shared by the department, if any discrepancy found, it is informed. Details of the document received shall be entered in the log as well as in the form of soft copy in the excel sheet by the QA Retrieval of records in the record room: When a record is requested, the QA personnel retrieves the document by referring to soft in excel. Simultaneously the document and record archival log is updated. Record room monitoring: Record room is monitored on a monthly basis by an authorized QA, where the documents and record archival log is monitored at least two weeks or prior to the end of every month. Upon completion of retention period of the document QA personnel shall fill in details of obsolete.

4. Line clearance

Line clearance is a method of assuring components, labels and documents from previous work/order/ activity have been removed and reconciled before beginning production of a new work order and to make certain the line is properly prepared for the next order.

Checking is to inspect the set line clearance parameters. Done by the person from user department.

Verification is the process to confirm something which is checked as true.

Line clearance assures that the area and equipment's are clean from any potential sources of cross-contamination or mix ups and also assure correct material are kept for use before beginning a specific operation.

Line clearance responsibility: QA personnel

Stages Of line clearance:

I. Cleaning of previous material

Documents/records, materials, rejects or any remnants of the previous work are cleared.

II. Cleaning

They are where the work will be conducted is cleaned

III. Arrangement required for new work order Relevant authorized copy, documents required to carry out line clearance process shall be available as per the document and record control. The work environment area condition is checked whether it is within the required limit. The area status/activity board is updated with the details (Product name, activity, Lot. No., Mfg. Date, etc.)

Cleaning of equipment's must be according to the SOP. Equipment ID must be mentioned in the line clearance document if applicable. Settings of the equipment's are adjusted according to the specification of process Ensure equipment's are calibrated and validated as per schedule and status is identified.

IV. Checking

V. QA verification

During clearance environmental conditions (temperature, humidity, etc.) and activity board are checked followed by checking of other parameters. Clearance is required at the following areas:

I. Manufacturing:

Calibration of equipment's

Raw materials required for the process and QC approved labels or requisition slips are verified.

II. Buffer/ Reagent Filling area:

The labels on the buffer containing bottles are verified is available.

Ensure QC approved label or release note Ensured raw material is arranged

Ensured label/ requisition slip is available.

III. Packing materials

Ensures packing materials are arranged Ensures QC approved label or release note is available.

IV. Packing:

Ensures packing materials are arranged Ensures QC approved label or release note is available.

Ensure Lot No/ A.r. No / Code /Serial no is entered

V. Dispatch area.

5. Log Book Verification

Log books: A bound spiral book used to record activities in various department. Log books are used for recording information relevant to machine operation, calibration, maintenance, and cleaning procedure that are performed on various equipment's. They are also used for recording information of the STP, SOP, Formats.

Log books are to determine good manufacturing practices required for traceability of data, events, communication. They are also important source of information.

Labelling and preparation of logbooks: The contents of the log books should be same as the respective controlled format or document. Every log book must be authorized by the QA personnel before the user department enters any data on the log book

A label on the must be present on the front cover with the following information Title of the log book (Equipment name/ process name/QMS related documentation procedure name) Log book ID (assigned by user department) Equipment ID, Additional details (For easy traceability).

Authorization of log books- The newly printed Log books are authorized by QA personnel by checking the format with proof reading copy provided by the user department. Which is followed by entering the following details on the first page of the log book: Effective date/w.e.f. date (With effective date) Reference

SOP/Document/STP No., Format no Revision No, Log book ID, No. of pages (of the log book) Authorization BY QA stamp, Address stamp.

Verification of Logbooks- Log books of all departments are verified by QA department twice every month, for any errors. The QA verifies the logbook and affixes QA verified Stamp. IPQA verifies logbook maintained by each department twice a month (beginning and middle of month plus or minus 4 days) i.e., every 15 days.

We were taken for logbook verification of extraction and PCR of QC department, where we verified logbook details, cross checked with checklist provided and verified the entries made.

6. Stability Report Verification

IPQA verifies stability reports of sample tested at various temperature at various time intervals by QC department.

Accelerated stability- it is performed at 45oC and 40oC with interval of 2 weeks and 1 month respectively. IPQA verifies details, cross check calculation and result of device result page.

7. Document Verification of Incoming materials

IPQA verifies incoming material details, vendors details and cross check nucleotide sequence of primers and probes.

8. Instrumentation verification

IPQA check functioning of machines, devices, physical parameters, bays and accessories. They cross check the results and software details.

Instrumentation of Trueprep device and packaging has to be done in the presence od QA officer, where they have to ensure that the details in the provided form are correct, serial numbers has to be verified, bays have to be checked manually and it should be free of dust and moisture. Trueprep device adaptors, cables, reagents bottles, cover, manus has to be packed.

9. Handling ON-LINE rejects

On line rejects are sort of applications that are prepared along with the material that needs to be rejected generated during manufacturing or packing process. The list is checked for on-line rejection reasons (atypical description, odour, atypical

clarity, colour, etc.), if any discrepancy is found within the material the concerned department files an on-line rejection note. On-line rejection notes are transferred to QA for their comments. QA assigns On-line rejection note (OLRN) No. and enters details in log register.

On-line rejection no: OLRN/OXX/YYY

O: Constant, XXX: Numerical character, YYY: Sequential No.

The online rejects are forwarded to QC department for comments, after reviewing rejection incidence, QC department affixes the rejected label after rejection is advised by GA head. The rejected raw material is transferred to store along with an inter-co, followed by transfer to quarantine room. QA evaluates the condition of balance stock of the rejected material and might also recommend for re-analysis. All the department heads decide whether to return the rejected material or to destroy it in premises. The original approved OLRN shall be retained by the QA department and a photocopy of it is provided to store.

10. Incident, deviation, change control and CAPA

Incident - it is raised when an event may or may not affect the product quality but it is against the product quality.

Deviation- it is raised when an event is against the protocol and it might affect the product quality.

Change control: is a systematic way by which any change is brought in the company. A change control form is filled to bring about any changes in the existing protocols. Corrective action, preventive action (CAPA)- these are the corrective actions which are used to correct any errors and the preventive action to prevent that error from occurring in future.

11. Facility validation report

Facility validation gives the documents necessary to demonstrates that facilities, utilities and process equipment's are operationally effective, safe and efficient. It helps to check whether all parameters are proper and as required by the process.

12. Review monitoring sheet

It is an excel sheet that helps to know revision number and distribution of SOP, STP, formats and lists to various departments. calibrated date and calibration due date of each and every.

13. Calibration calendar

It is an excel sheet that has equipment.

14. Maintenance of calibration report

It is a kind of certificate that gives the details of the equipment along with the calibration date and calibration due date.

Good documentation practices

It is a term used to describe standards by which documents are created and maintained. It helps to understand who, when, where, why, how to complete relevant activity and provide evidence to show whether these have been completed as expected.

ALCOA- key to GDP (frame work for ensuring data integrity)

A-ATTRUBUTABLE (Entries shall be dated on the date of entry and signed)

L-LEGIBLE (Data shall be recorded directly and promptly) generated)

C-CONTEMPORANEOUS (Data shall be recorded at the time it is O-ORIGINAL (First record made by the person)

A-ACCURATE (Confirming exactly to the truth)

All documents must be on an A-4 size white paper, with data printed in black.

All documents must be filled with blue ball point pen.

Handwritten signature must be unique and must be registered in the master signature list.

Date and time: 24:00 Hrs format in HH:MM

DD/MM/YYYY OR DD/MM/YY

The document must contain the following: Title (Concise and clear)

Identification number (helps in identification)

Page No. (A of Z-A is sequential no, 2-total no of pages)

Revision number

Data recording: All entries shall be recorded in the format issued and approved by QA in the log book must be in a chronological order and shall never be filled before the completion of actual activity If any observation is to be repeated it has to be written and the use of "is not allowed. Use of peak symbol for additional entry shall not be used

All documents must have an entry, if the column does not require entry NA must be written and the space must not be left blank.

If any space needs to be left blank a diagonal line must be drawn and NA with signature be written.

For correction of any mistake, overwriting is not allowed, instead a single strike should be made out let the entry readable. Correct entry should be written next to strike out entry with date and sign. Reason for correction shall be mentioned. In case of space constraint * sign should be made near the error and the reason should be mentioned wherever the space is available.

Standard testing procedure

STP is a process that is used to design, co-ordinate and analyse a laboratory testing procedure.

The format of standard testing procedure includes: Header: Includes company name, location, and state.

Title, department, page no., STP no., revision No., effective No., CC No., Checked by, prepared by, approved by in a tabular column.

Body: Objective, scope, responsibility, accountability, reference, attachments, Materials required, procedure, additional section (reporting), amendment details, precaution, abbreviations.

Footer: Includes a statement (This document is the property of Molbio Diagnostics Pvt. Ltd. Goa. It must be handled as classified and not derived or recreated, in whole or in any parts in any way without the permission of the company)

Preparation of STP:

It is prepared by the respective user department.

Draft copy of the STP is circulated to the concern department for corrections/ modification/comments. 3. All the required changes are made after receiving the comments.

Draft copy is destroyed, fresh printout is signed by the person preparing it, checking Training is conducted of the respective STP and person responsible for it.

An effective date is assigned to the STP after training. 7. The STP is submitted to the QA department, if any mistake's found corrections are made.

Review period of STP is 2 years.

Production Department

We were further given induction sessions on how the production departments functions, and how its work is also linked to the Quality control department. A brief description on how the production department is as follows.

Induction given by: Mr. Gitesh

1. **Chip Sorting room**

   1 tray contains 240 chips

   Count for exact number of chips- QA gives line clearance- sorting is done- approved/rejected- transfer to washing.

2. **Washing room**

   Here the Truenat chips are washed thoroughly to avoid any contamination in the final product. Air pressure along with electro-deionised water and ultra-pure water is used alternatively for washing.

3. **Oven Drying**

   The chips are then incubated in ovens (80oC for 20mins) and then transferred into UV chambers (20mins).

4. **Mg Preparation room**

   In the ceramic well of the Truenat chip, 2 types of coats are dispensed; the BSA coat and the hydrophilic coat.

   10µl of BSA is first added into the well to fill up any pores and make the surface smooth. The hydrophilic coat is then added which contains, 10% tween20, 40% trehalose, 50% glycerol and 50 mM MgC12. MgC12 is used in the coat mix which lines the walls of the well. In PCR. MgCl2 is an essential cofactor that enhances the activity of Taq DNA polymerase, which in turn increases the amplification rate DNA. Coat dispensing is done by Bidot Reagent Dispensing Machine.

5. **Polymer/Wax filling room**

   Induction by Mr. Manjunath

   Wax is first melted on a hot magnetic plate and then filtered to remove any contamination. It is then filled in a tube dispenser which dispenses 5.8 to 6.2 mg

of wax in the well. The wax is then allowed to dry. To check if there is any remaining moisture content in the well, a device called the Coulometer is used.

6. **Biomix Area**

   Induction given by: Ms. Shweta

   The liquidated master mix is created in this room. This master mix contains of primers, probes, buffers all in the right proportions. Trehalose is also added to the master mix for stability during freeze drying. At every step of preparation, a sample is sent to QC department for quality check. Preparation of the master mix is done in cold conditions as the enzymes and buffers used are heat specific.

7. **Flash writing room**

   After dispensing of the coat and the wax into the well, the chips are sent to be flash-written. The chip consists of a Flash Memory (16 bytes) which contains its lot number, the disease specific ID, and 3 slope values which are essential for reading by the micro-PCR analyser.

8. **Lyophilisation room**

   Here the liquid master mix is subjected to lyophilisation/ freeze drying. Lyophilisation is the process in which water is removed from a product after it is frozen and placed under = vacuum, allowing the ice to change directly from solid to vapor without passing through a liquid phase. The entire process takes 42 hours.

9. **Pouching and Packaging room**

   The final lyophilised master mix tubes, the coated chips, and the pipette tip are then pouched in sleeves which are then sealed into pouches containing a silica gel packet to absorb moisture. These are then packaged according to requirements.

Conclusion

In the course of 30 days of internship in Molbio Diagnostics, I was able to gain a lot of insightful information on the diagnostic methods and devices used to diagnose many different diseases like Covid- 19, HAV, HBV, HEV, MTB. Etc. I got to learn the functioning of a diagnostic company, how it works on an industrial scale, and all the sectors associated with it, along with practical training on how to operate various laboratory-oriented devices and documentation. It provided me an insight on professional practice.

As an intern in QA department, I had an exposure in all fields and was trained and given idea about role of QA department in a manufacturing company.

The internship was a very useful exposure as it enabled me to develop and master new skills through training. Over all it was a pleasant learning experience.

I would like to thank Molbio Diagnostics Private Limited for giving all support and opportunity for this knowledgeable internship.