MOLECULAR DIAGNOSTICS : QUALITY ASSURANCE CHALLENGES

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Lab assistant to Lab Technologist

Scientist MMed Science/ PhD - Molecular Virology 2002

Current Lab – 11 sites across the Country

36 000 samples per Month

Test profiles (all types, HPLC/MS; NGS) Clinical pathology … Molecular Biology

Trainer Registrars /Medical Technologists

Auditor Sanas and HPCSA

BACKGROUND

- NHLS/ State Labs – 25 years - Large personnel – 5000 samples a day – always short of money
- MRC / Clinical Research – FDA Drug studies -
- Private/ Academic Lab - 392 Staff complement – Madly competitive/ Hectic deliverables / Quality Assurance is the Key to Patient care

PRESENTATION OVERVIEW

- Over view of Quality Assurance
- The Lean Principle as an AID to Improve Medical Laboratory Quality
- People ….People…. People Key To Quality
- Candid Quality Control Challenges in Molecular Biology , what's different from other laboratory Tests
- Responsibility to ensure Quality, Some of our Own Initiatives – Did it Work

QUALITY ASSURANCE : COVERS 1-10

GOOD LABORATORY PRACTICES PRINCIPLES.

1. Test Facility Organisation and Personnel.
2. Quality Assurance Programme(QAP).
3. Facilities.
4. Apparatus, Material and Reagents.
5. Test systems.
6. Test and Reference Substances.
7. Standard Operating Procedures(SOP).
8. Performance of The Study.
9. Reporting of Study Results.
10. Storage and Retention of Records and materials.

LABORATORY HAS 3 MAJOR COMPONENTS

DEFINE A LABORATORY

- A LAB IS A COURIER CONTROLLED SERVICE

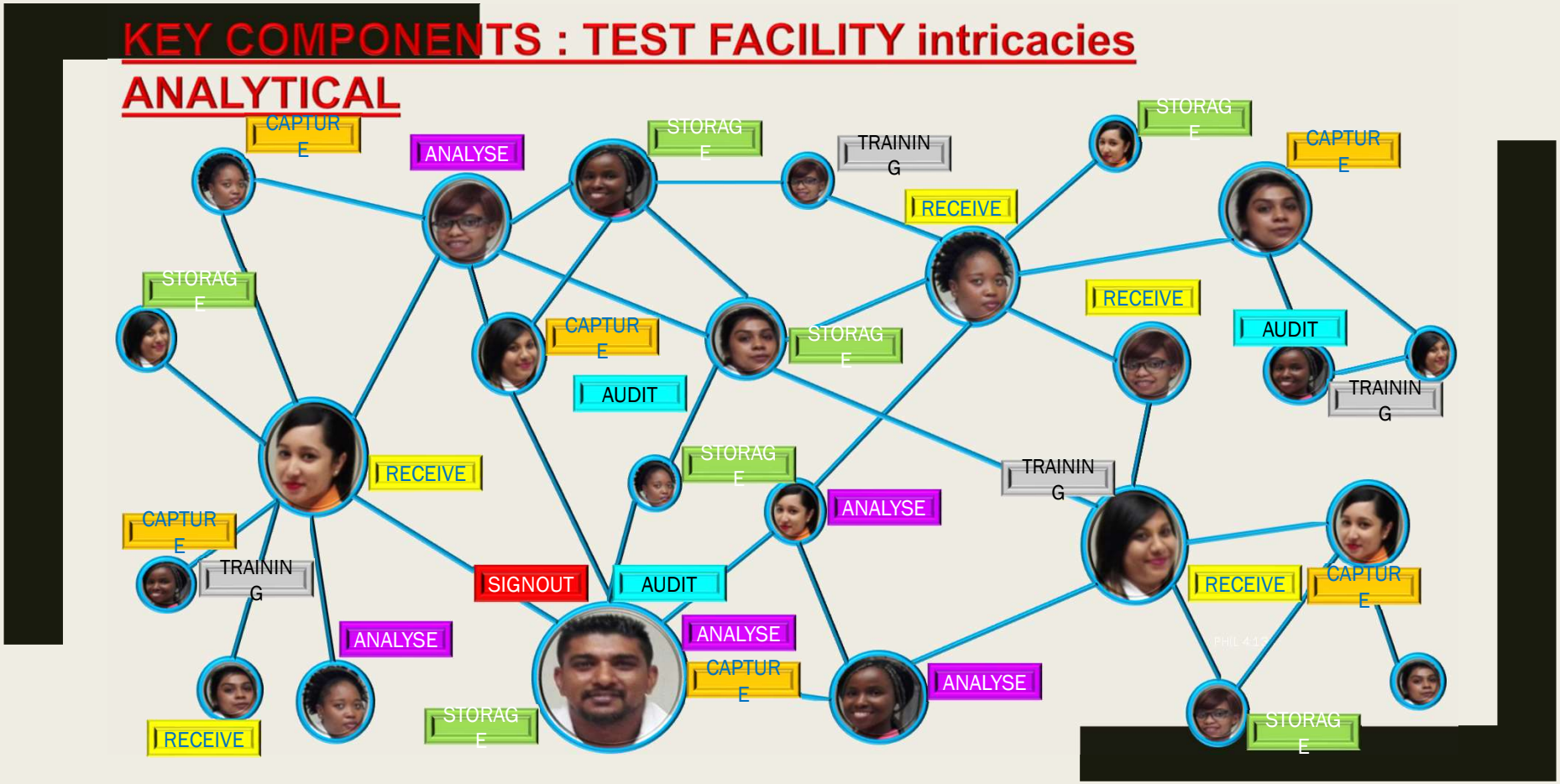
Hence Where DOES QUALITY START

LABS Donot TAKE RESPONSIBILITY for THE PREANALYTICAL PROCESSES

(LABS QUALITY STARTS AT THIS STAGE)

KEY COMPONENTS : TEST FACILITY intricacies

ANALYTICAL



KEY COMPONENTS

3. Facilities

- **Suitable size, construction and location.**
- **Adequate degree of separation of the different activities.**
- **Isolation of test systems and individual projects to protect from biological hazards.**
- **Suitable rooms for the diagnosis, treatment and control of diseases.**
- **Storage rooms.**

4. Apparatus, Materials and Reagents

- Apparatus of appropriate design and adequate capacity.
- Documented Inspection, cleaning, maintenance and calibration of apparatus.
- Apparatus and materials not to interfere with the test systems.
- Chemicals, reagent and solutions should be labeled to indicate identity, expiry and specific storage instructions.

KEY COMPONENTS

5. Test Systems

- Physical and chemical test systems.
- Biological test systems.
- Records of source, date of arrival, and arrival conditions of test systems.
- Proper identification of test systems in their container or when removed.
- Cleaning and sanitization of containers.
- Pest control agents to be documented.

6. Test and Reference Items

- **Receipt, handling, sampling and storage**
- **Characterization.**
- **Known stability of test and reference items.**
- **Stability of the test item in its vehicle (container).**
- **Experiments to determine stability in tank mixers used in the field studies.**
- **Samples for analytical purposes for each batch.**

KEY COMPONENTS
SOPs working documents – Not a filing cabinet

7.Standard Operating Procedures (SOP)

- Written procedures for a laboratories program.
- They define how to carry out protocol-specified activities.
- Most often written in a chronological listing of action steps.
- They are written to explain how the procedures are suppose to work.

7.SOP's

- Routine inspection, cleaning, maintenance, testing and calibration.
- Actions to be taken in response to equipment failure.
- Keeping records, reporting, storage, mixing, and retrieval of data.
- Definition of raw data.
- Analytical methods.

LEAN PRINCIPLE APPLIED IN A MEDICAL LAB

- Finding the approach to use Lean Principles to be easy, efficient and cost saving as well
- In simple Terms **Implementing Logical approaches**
- We also finding that High Quality labs are already using the Lean Principles without Realizing it

LEAN PRINCIPLE AS A TOOL FOR A MEDICAL LAB

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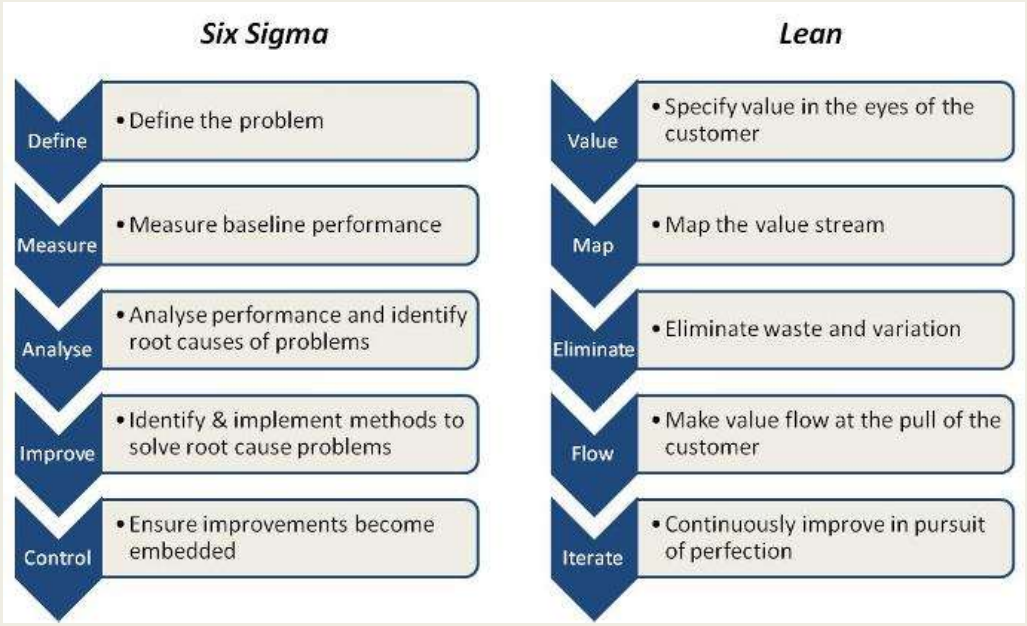
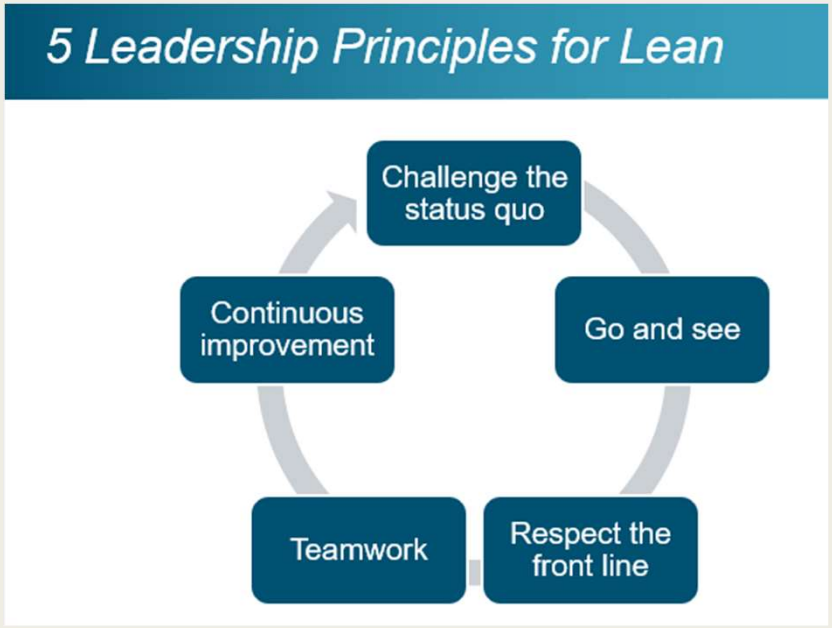
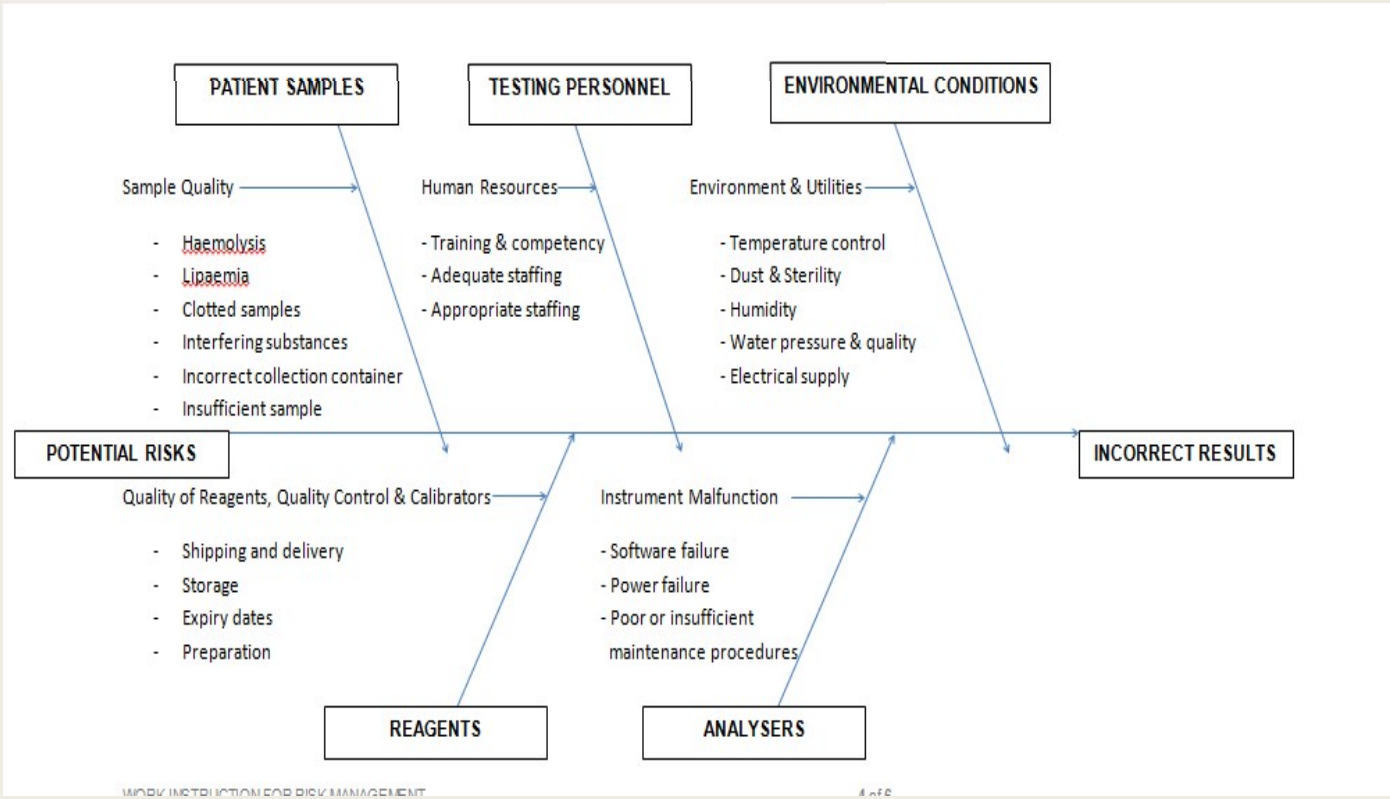


WE ALL KNOW THIS



*RISK ASSESSMENT



Alignment of Six Lean Principles

Source: Adopted from Lean Academy™, 2008

People…Employees ….staff… directors

- STAFF CAN CREATE THE WORST QUALITY ASSURANCE issues
- The General assistants – trained to Remove Molecular waste –

People...Employees ...support/staff .. domestics....LAB techs... directors

Quality Control Challenges in Molecular Biology

- Main Challenge in this Field is the failure to Highlight and Bring to the For Problems with other Peer Labs performing Similar work
- Insecurity of Scientists and Lab techs –
- Problems discussed as a group is lessened , jointly we can come up with PROPER Solutions

QUALITY ASSURANCE ISSUES IN A MOLECULAR LAB

- Are molecular diagnostics immune from quality problems? Or excluded from Quality Assurance
- Do they need Quality Control?/ assurance
- In this new field of testing, methods and manufacturers have been aserting their "difference" from traditional testing practices, while moving slowly on developing any new and different quality practices

PREANALTYICAL PROBLEMS....COMMONLY THE INIATOR OF ALL LAB PROBLEMS

- (incorrect sample; inaccurate sample labelling; poor sample collection, inadequate sample tracking ; inappropriate sample transport)

- POOR CHAIN OF CUSTODY / INADEQUATE MONITORING PROCESSES)

Answer Use Technology to support eg Electronic Temp Monitoring; Electronic tracking etc) Is the sample Integrity Intact

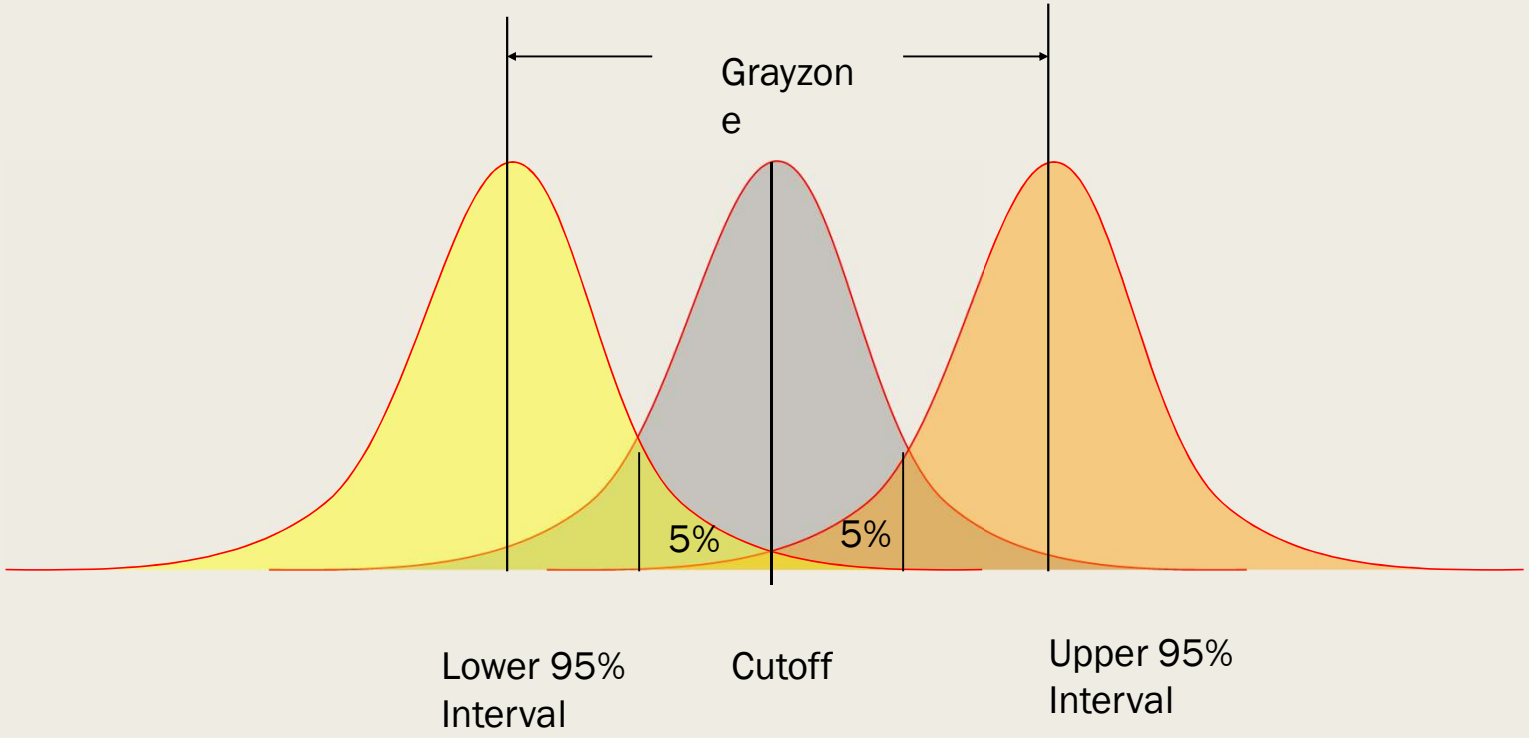
TYPICAL MOLECULAR LAB ….

- Few fully automated systems, mostly developed testing algorithms
- HIV1/2, TB , (infectious diseases) – commercial influence- large volumes hence HIGH automation high QC implementation
- Several diseases still rely on Peer reviewed publications (see if the authors are willing to support /help you with setting up assays that they have published)

QUALITY ASSURANCE ISSUES IN A MOLECULAR LAB

- Tests are new and rapidly evolving technologies
- High expectations of accuracy for once in a lifetime genetic tests
- Lack of quality control materials,
- Lack of quantitative test system outputs,
- Westgard the Guru For QA in Medical labs , ? How far is he with Molecular Testing

CAN THIS WORK FOR MOLECULAR BIOLOGY



FACE the FACTS

- Several Molecular tests are done manually only High Request tests get attention
- Conventional Molecular assays : Results were determined by interpreting the presence or absence of bands on a gel. Such testing was often performed by researchers with minimal experience in traditional QC techniques, and the QC materials consisted of previously tested patient samples. Monitoring for systematic errors was deemed to be unnecessary because test failure was easily detected. Furthermore, since the QC materials were variable, labs did not know if a change in band intensity meant an enzyme was degrading or the selected patient control samples did not contain enough DNA.. .....

(Several molecular tests are still in this process of running gels) – can they be implemented as diagnostic tests at this stage YET some of these assays have Huge Diagnostic use, especially Genetic diseases

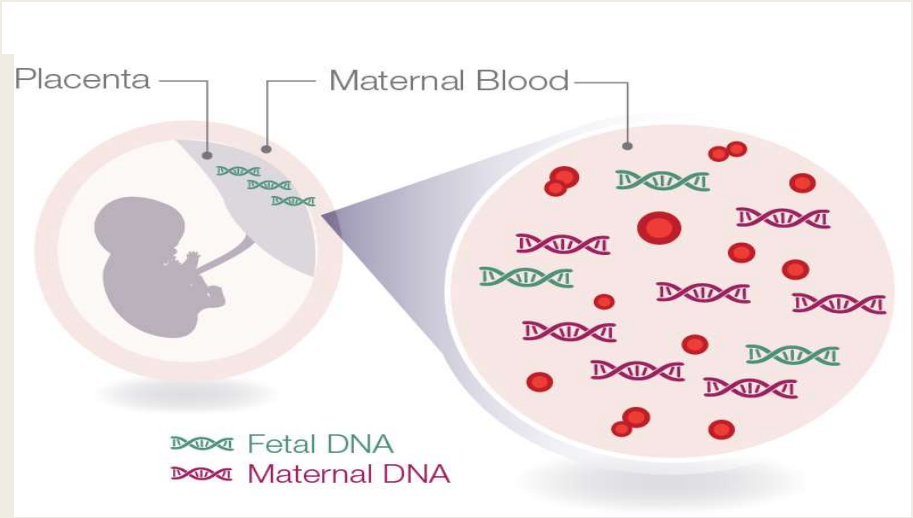
FACE the FACTS

- Limited commercial availability of QC materials
- Some labs also pool patient samples to create a reproducible source of such materials. (DIFFICULT)

FACE THE FACTS

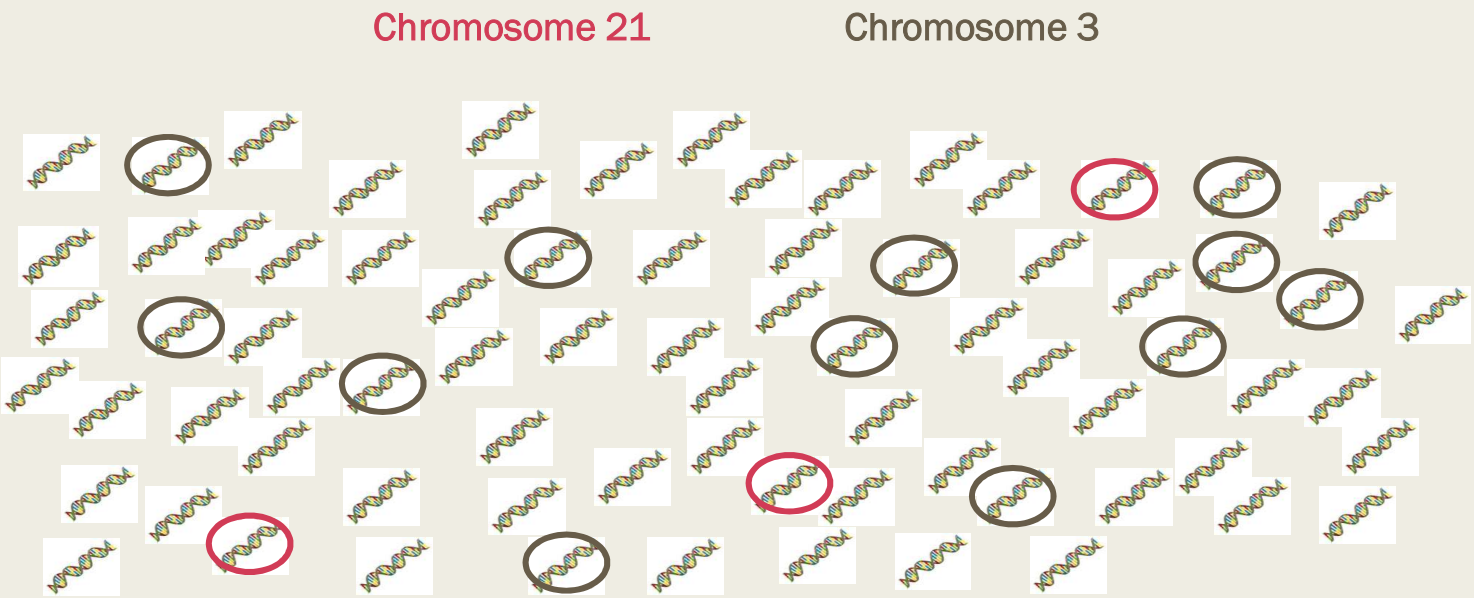
- Molecular life is about to become further complicated as even more complex tests—Next Generation Sequencing (NGS),
- RNA and DNA microarrays,
  - *Mass spectrophotometry*
  - *These complex platforms test a variety of human specimen types for sometimes thousands of analytes—potentially the entire human coding genome of approximately 22,000 genes – HOW WILL WE IMPLEMENT QC IN THIS ASSAY*
- Multiplex PCR - In each patient sample run, current QC practices for multiplex tests involve testing two to three QC samples, each representing at most two alleles However, this practice does not ensure that all alleles of a multiplex test are being detected correctly in each run.

FACE THE FACTS – intricacies of molecular testing (That cover all aspects of the test)



Face the Facts

Counting



FACE the Facts - ERROR RATE

- A CDC report found that molecular diagnostic test error rates are largely unknown.[4] The limited amount of proficiency testing (PT) data for molecular diagnostics provides the only information available for assessing laboratory errors

- In most commercial assays we have options of using variable kit types to verify results eg If an HIV rapid test is performed using Lateral Flow testing, A verification assay can be performed eg ELISA automated assay to confirm
- Molecular Tests have not reached such a THOUGHT PROCESS- This is Vital.

Responsibility to ensure Quality, Some of our Own Initiatives – Did it Work

- Elements needed to bring molecular QC practice up to the same level as other laboratory disciplines:

Determining error rates – analyse your data and results frequently and accept that there are inadequacies that need to be Fixed

Liaise with Clinicians to discuss probabilities of the lab tests being correct

Adopting traditional QC protocols to monitor system performance in order to prevent failure, develop your own Intellect , But never fail to share it with Colleagues

QC materials useful for generating data for system monitoring and error prevention, create your own pool BUT Validate with other Peer Colleagues

Increase proficiency requirements and samples for molecular tests

INTERNAL AUDITS

INIATIVES TO CREATE A QUALITY MANAGEMENT SYSTEM FOR MOL BIOLOGY

- Laboratory Buddies works best ; Has to be minimum of 3 labs in this process
- Scientists Network
- Share skills
- Share Sops
- Share Challenges

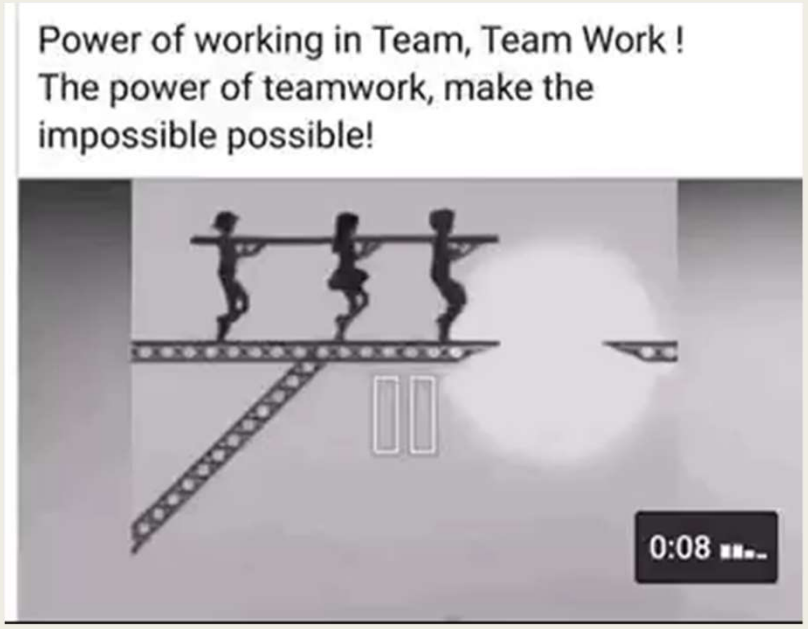
Share Quality assurance material, create QA programmes – within labs, outside labs

Seek advice from CDC/ Westgard/ College of American pathologists

(NEVER FAIL TO SHARE YOUR CHALLENGES AND PROBLEMS; you will be surprised the others have the same)

WORKING TOGETHER IMPROVES QUALITY

THE ONLY WAY


Power of working in Team, Team Work !
The power of teamwork, make the impossible possible!
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PLEASE FOLLOW THIS PRINCIPLE
TEAM WORK

- **BE** - FIRST
- **DO** - BE A DOER, get the knowledge , run the tests yourself, calculate the results
- **SEE** – BEFORE YOU COMMENT
- **TELL** /INSTRUCT –

- *(Create a Morale in the lab where people will bring up the problems*)

FINAL COMMENT

- Its not an easy Task to ensure that You Implement a Stringent Quality System But It is Highly Possible

THANK YOU

ORGANIZORS OF AFRICA HEALTH

PROF TS PILLAY

IQBAL