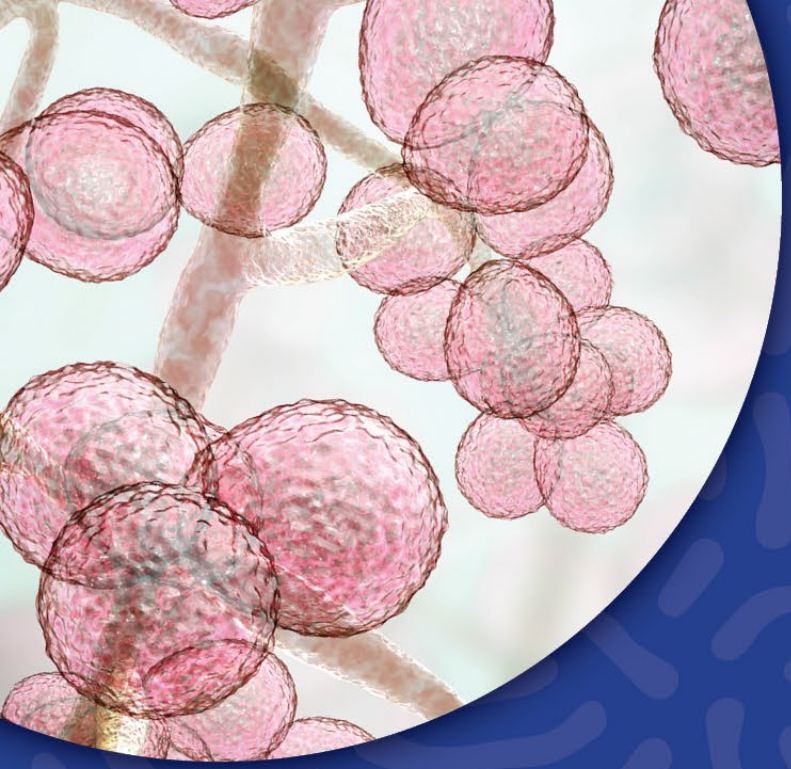

ID LAB CON

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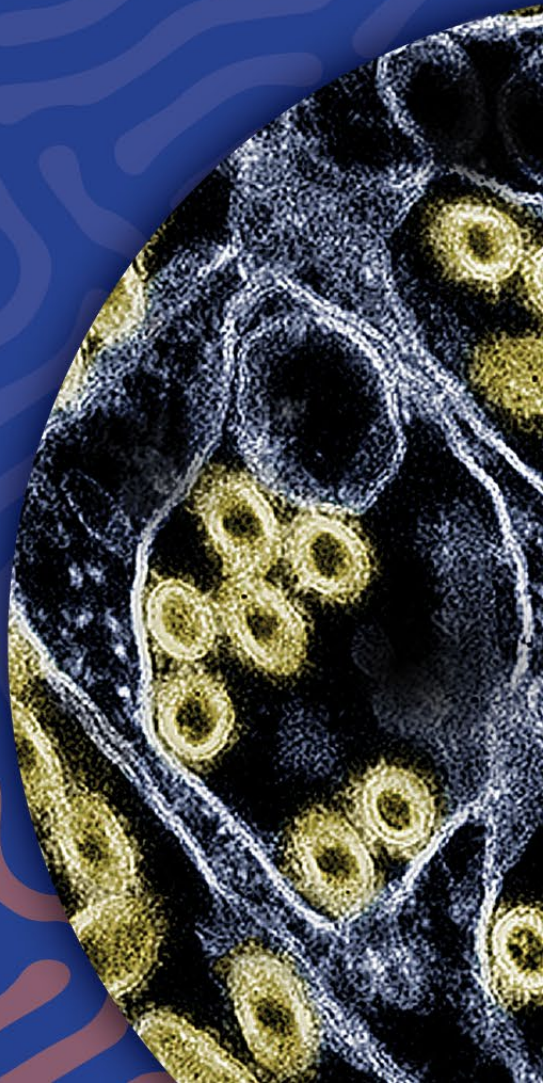


Quality Management Systems in Next Generation Sequencing

#IDLabCon

Noah Hull

Global Health NGS Team

Global Health, Association of Public Health Laboratories

Conflict of Interest

The authors and presenter do not have any conflicts of interest.

The views presented here are those of the presenter and not those of the funder or of APHL.

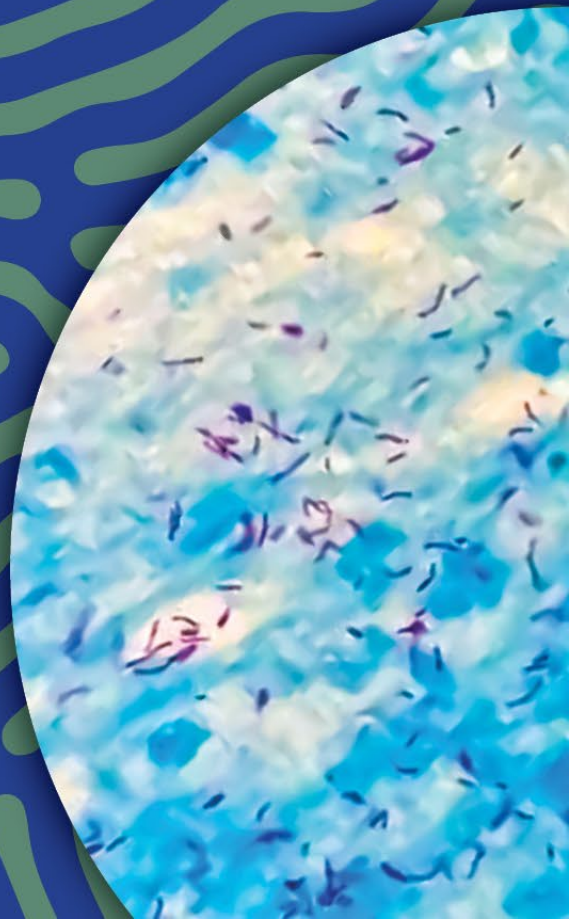


Table of Content

Why Do We Study Infectious Diseases

Local and Global Implications

- In the U.S., infectious diseases widen health disparities and place a substantial toll on healthcare resources (Khabbaz et al., 2014).
- Collier et al. (2021) estimated that in a year, the United States spends $3.33 billion in direct healthcare costs associated with waterborne infectious diseases.
- Infectious diseases is the leading cause of child mortality in low-income countries (Baylor College of Medicine, n.d.).

Infectious disease challenges in the USA

(Khabbaz et al., 2014)

- Vaccine-preventable diseases are on the rise - **United States spends an estimated $27 billion annually for adult VPDs treatment (Kolobova et al., 2022)**
- Health-care-associated infections (HAIs) - **$26–33 billion in excess medical costs and around 99,000 deaths yearly**
- Foodborne infections - **Every year, around 48 million foodborne illnesses occur in the USA, resulting in 128,000 admissions to hospital and 3,000 deaths**
- Chronic viral hepatitis - **Around 800,000 – 1.4 million people in the USA are chronically infected with hepatitis B virus (HBV) and 2.7–3.9 million have chronic hepatitis C virus (HCV)**
- Tuberculosis – **There are ~11 million people in the USA with latent tuberculosis infection**
- Antimicrobial-resistant pathogens - **The CDC estimated that AMR is $55 billion annually in the United States, $20 billion for health care, and about $35 billion for loss of productivity (Dadgostar, 2019)**
- HIV, and sexually transmitted infections (STIs) - **Around 20 million newly acquired STIs occur every year in the USA, resulting in about $16 billion in healthcare costs**

How Disease is Measured

Epidemiologists and Public Health Professionals

- The cornerstone of epidemiology and health is “measurement”. Measurement in diseases (specifically infectious diseases), can only be measured after epidemiologists have composed a CASE DEFINITION for the disease. In infectious diseases, This DEFINITION is based on but not limited to physical and pathological examination and diagnostic testing (Aschengrau & Seage, 2020, p. 37)

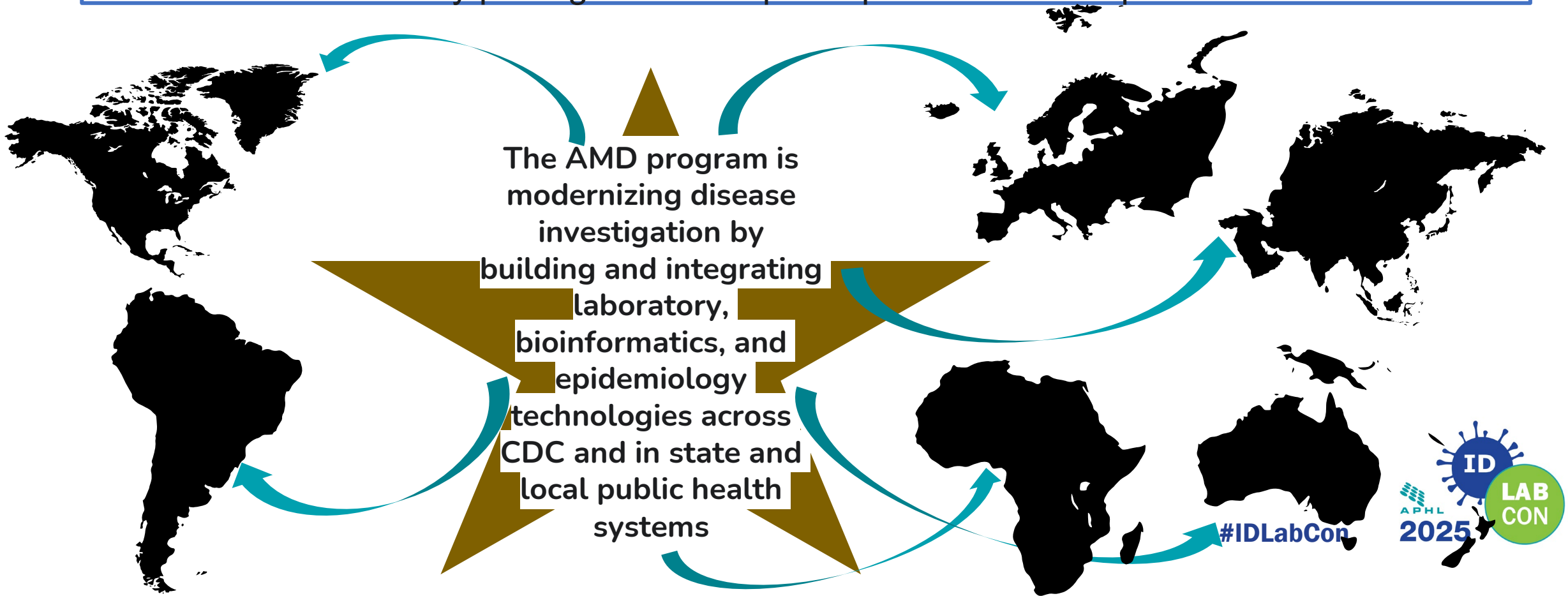
- Public health professionals use the two basic measures of diseases frequency, Incidence and Prevalence, to measure how new and existing diseases are occurring. This measurement in recent years has relied on **molecular detection.**

In 2014, the **Advanced Molecular Detection (AMD)** was established to protect Americans from infectious disease threats, through the integration of **pathogen genome sequencing** into **disease surveillance** (Gwinn & Armstrong, 2019)

Impact of AMD on Public Health (CDC, 2024)

Roadmap to Global Health

The purpose of AMD Advanced molecular detection (AMD) is to harnesses the power of next-generation genomic sequencing, high-performance computing, and epidemiology to study pathogens and improve public health response.



The Underlying Factor

Keeping an eye on the prize

SEQUENCING

Next Generation Sequencing (NGS)

Next-generation sequencing (NGS) is a technology that reveals the sequence of DNA or RNA

- In infectious disease surveillance, **sequencing** plays a major role in tracking variants, pathogen dynamics, and spread.
- “In recent years, **NGS** technologies has allowed rapid, precise, accurate, and cost-effective characterization of pathogens to support clinical interventions and public health responses” (Morse & Pillai, 2024)

What is Quality Management Systems

A quality management system is a clearly defined set of processes and responsibilities that guides operational practices (ISO, n.d.).

TRUST IN THE RESULTS

Customer Satisfaction

- Implementing quality standards is the cornerstone for generating quality results (Hutchins et al., 2019).
- Next-generation sequencing (NGS) has revolutionized clinical diagnostics and public health diseases exploration (Yadav et al., 2023)

What is QMS in NGS?

A quality management system is a clearly defined set of processes and responsibilities that guides operational practices (ISO, n.d.).

Next-generation sequencing (NGS) is a technology that reveals the sequence of DNA or RNA

A quality management system in NGS is a clearly defined set of NGS processes, guidelines, methods, and responsibilities that guide sequencing operations and workflow from extraction, wet laboratory and dry laboratory procedures.

Budowle et al. (2014) stated that NGS results significantly impact how officials investigate public health threats. Therefore, accurate and credible results are imperative.

Why QMS in NGS is Needed?

Quality control measures ensure the accuracy, reproducibility, and reliability of NGS data.

- It ensures that tests results are accurate, reliable, and reproducible.
- NGS methods and processes are challenging, and the margin of error is very small due to the sensitivity of the process and design.
- Quality assurance is critical in laboratory processes as it establishes standards for laboratory practices and procedures
- Whole genome sequencing data is only as good as the quality of sequences (Morse & Pillai, 2024).

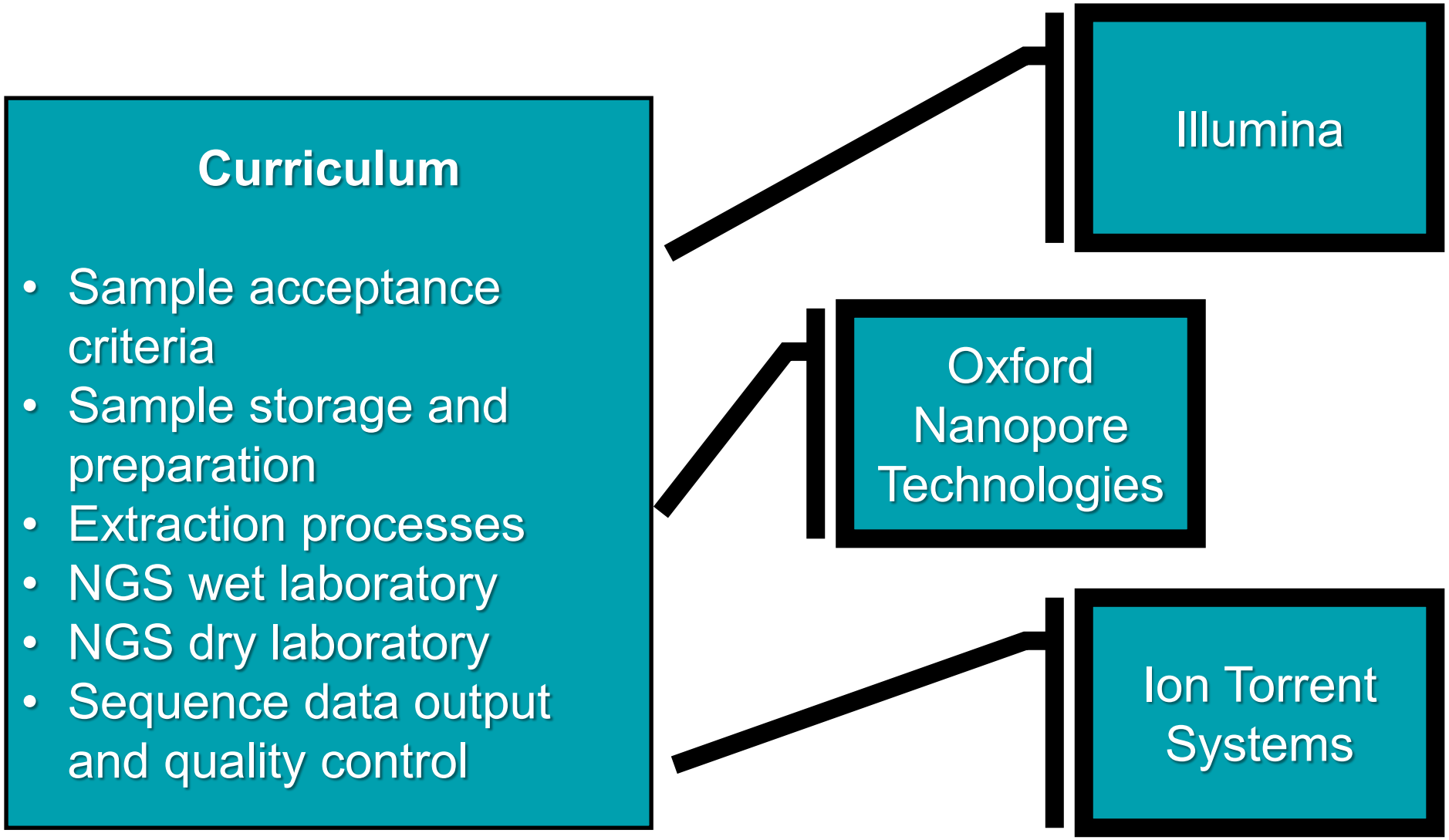
Instructional Design Framework of NGS

- Sample acceptance criteria
- Sample storage and preparation
- Extraction processes
- NGS wet laboratory
- NGS dry laboratory
- Sequence data output and quality control

The APHL QMS in NGS curriculum addresses **sample reception** and **extraction processes.**

NGS can not be conducted if the extraction step fails quality control checks.

QMS in NGS Curriculum



Training Platform

Classroom

Home
Calendar
Teaching
To review
APHL/CDC NGS, QMS, and B...
Accra, Ghana
Quality Management in Next...
Maputo, Mozambique
Quality Management in Next...
Nairobi, Kenya
Archived classes
Settings

Introducing Generative AI for Educators

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The outcome of NGS in QMS Training

Mozambique

- Design validation/verification methods for next generation sequencing (NGS)
- Apply quality management system (QMS) principles to NGS
- Differentiate between method evaluation plan, validation and verification
- Apply quality control and assurance to the Illumina NGS workflow
- Identify quality issues in NGS data and areas for improvement
- Develop QMS guidelines for NGS

Long-term future goals for NGS in QMS Training

- **Development of a QMS in NGS Implementation guidelines and manual to provide guidance to all NGS laboratories:**
- For lab setup requirements
- Sample transport guidance
- Extraction
- NGS set up
- Reporting
- Accreditation guidelines, ISO 17025, 15189, 8000-1, and 8000-51
- Virtual asynchronous format (Kenya for ONT)

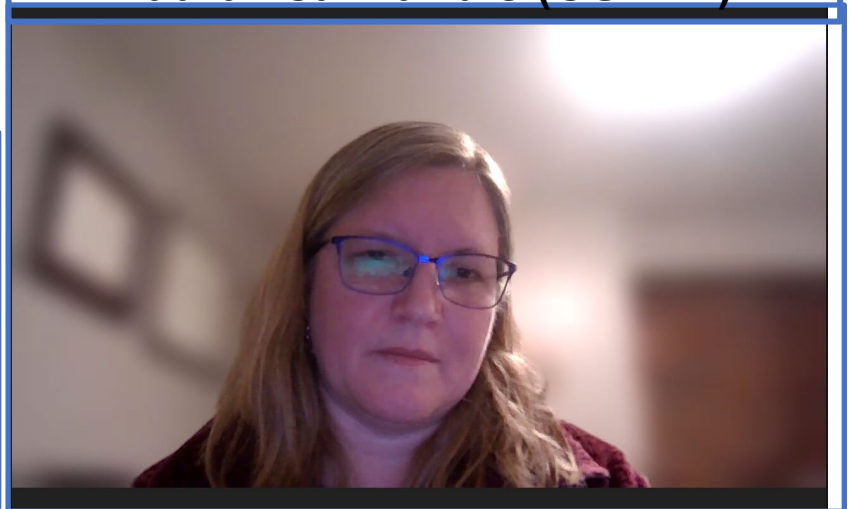
QMS in NGS Training in Kenya

Opening Ceremony

Dr. Peter Thairu & Dr. Nthiga (Illumina Channel Partner F&S Kenya)

Working Group Sessions

Sheri Hearns, Vanda Makris and Laura Tsaknaridis (OSPHL)



- Invited experts on Quality Management Systems to lead round table discussions
- Invited technical experts on sequencing platforms for instrument-specific QA/QC
- Hands-on application of QMS in NGS

QMS in NGS Training in Mozambique

Participants lead discussions

Round table discussions

Closing ceremony

Empowering laboratorians and quality officers to lead QMS training in provincial laboratories in Mozambique.

QMS NGS Training in Ghana

Training participant teach back and review of previous day lectures (to ensure participants understand the concepts)

Opening ceremony with participants

Hands-on practical approach to NGS best practices and contamination reduction

Meeting Training Objectives - Ghana

Obj.	Projected Learning Objectives	Learning Objectives Outcome	Evidence
1	Define (or apply) sample acceptance criteria for NGS	Participants learned to develop sample acceptance criteria for their NGS assay based on the validation results	Successful method evaluation plan development and validation report
2	Apply quality management principles, including lab safety and quality control	Participants learned to create quality control metrics and charts for their NGS workflows based on their validation reports for laboratory assays	Laboratory staff set thresholds and guidelines for where appropriate QC should be verified before the next sequencing steps can proceed.
3	Interpret a FASTQC report to assess the quality of NGS data	Participants were able to successfully run fastqc on Galaxy and interpret the fastqc report	Participants were able to use Galaxy to assess the quality of SARS-CoV-2 fastq files by running fastqc and using the results to trim low-quality reads

Meeting Training Objectives - continued

Obj	Projected Learning	Learning Objectives Outcome	Evidence
4	Develop self-owned SOPs and procedures for protocol method evaluation, verification, and validation in the laboratory	The laboratory scientists reviewed the IMAP protocol and changed the steps to align with the laboratory's setup and workflow.	Automation of master mix calculations and re-ordering protocol steps to minimize contamination and user errors during library preparation.
5	Outline proper data management of testing results	Participants discussed a strategy for safely importing and transporting sequenced data from the iSeq100 to bioinformatics workstations for analysis.	Initial discussion of data management protocol for NGS
6	Incorporate characterized genomic data into a validation and verification report to capture accuracy, sensitivity, specificity, and limit of detection of NGS assays	Participants learned about the difference between validation and verification in the context of quality management and accreditation standards and had hands-on practice in developing a validation report	Participants successfully created a validation report for the IMAP assay on sequencing SARS-CoV-2 and 16S.

Participants Share Their Stories (direct quotes)

I really appreciated it and hope a follow-up will be held. - Mozambique

The workshop was very good, I learned a lot about QMS in NGS. And I say thank you for coming, I really appreciate. - Mozambique

Insightful and Fantastic training! - Ghana

This Training is more productive than all the other trainings I have had bioinformatics. I have learned, understood and can practice almost everything that has been taught - Kenya

The training lived up to my expectations. The timing of the sessions was good; The duration of the sessions was also good; The training material was ideal for the purpose of the training; The facilitators have extensive knowledge of the training material, which was good for the success of the training. - Mozambique

Thanks to the funders, organizers and the facilitators for this wonderful knowledge they have imparted to us.- Ghana

Participants Share Their Stories (direct quotes)

"Another crucial aspect of the training focused on **Quality Management Systems (QMS) in NGS** laboratories. We learned the importance of implementing robust QMS to prevent contamination, ensure the integrity of our libraries, and consistently produce high-quality sequencing data.

This training has been one of the best bioinformatics and NGS-focused experiences I've had. The knowledge and skills acquired will greatly enhance the capacity of NPHRL to conduct genomic sequencing efficiently and accurately, ultimately strengthening public health interventions."

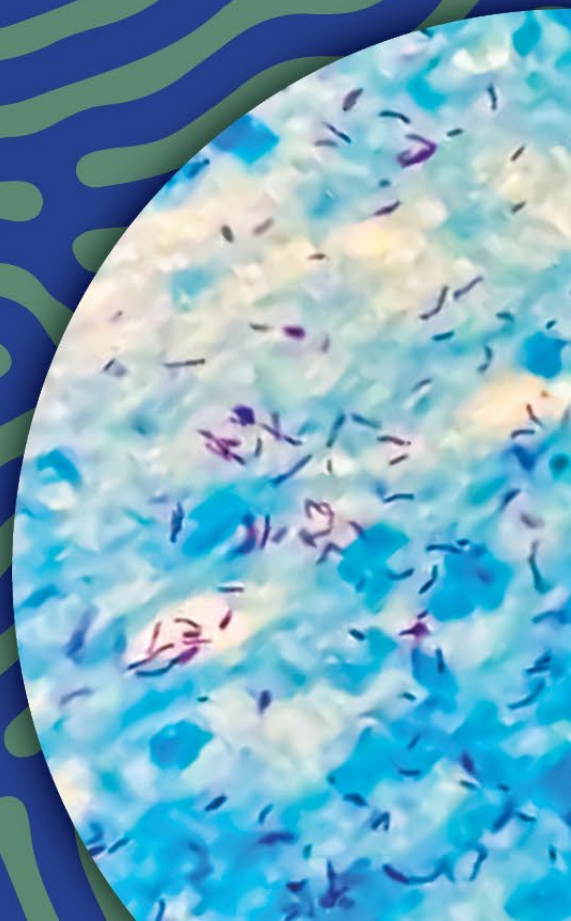
Joycelene (Akua) Attu
Medical laboratory Scientist, NPHRL, Ghana
Participants in "QMS in NGS Training, Accra, Ghana"

Conclusion

Molecular testing is essential in the realm of infectious disease.

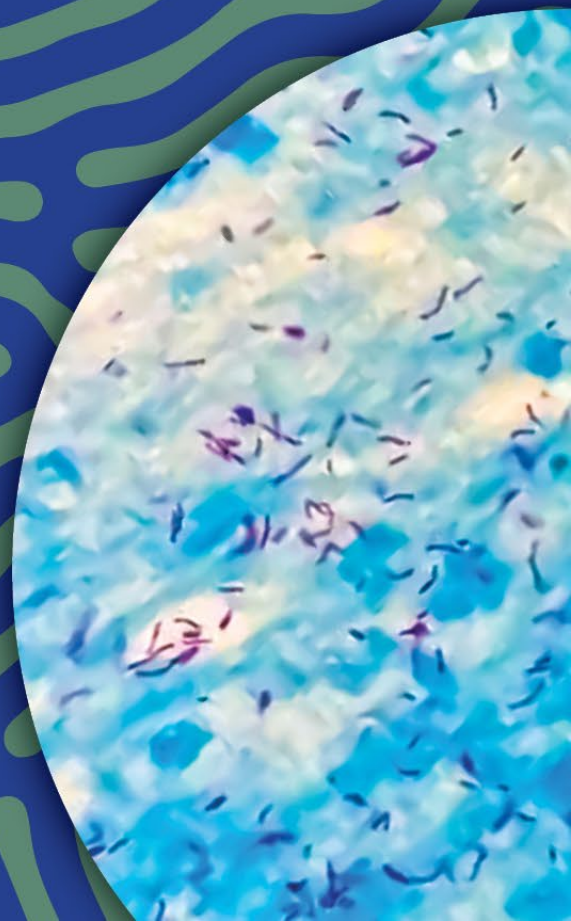
It is crucial for getting accurate results, identifying mutations, detecting infectious agents, understanding disease mechanics, studying patterns of diseases, monitoring pathogen spread, detecting drug resistance, and informing disease trends.

As a result, it is paramount that the results are accurate. Inaccurate results or incorrect characterization can lead to severe consequences that may lead to detrimental outcomes to both individuals, community, and the society at large.



Thank You!

U.S. CDC
CDC – Kenya
CDC – Mozambique
CDC - Ghana
Kenya National Public Health Laboratory
Mozambique National Institute of Health (INS)
Oregon State Public Health Laboratory
APHL Global Health and Global Health NGS Team
F&S Scientific - Kenya



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