# Comparison of Whole Genome Sequencing Between the Manual Illumina MiSeq™ System and the Automated Clear Labs Clear Dx™ to Support the Antimicrobial Resistance Laboratory Network.

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## Background

Antimicrobial resistance is of increasing concern and the ability to rapidly detect resistance in healthcare-associated infections (HAIs) is of vital importance to prevent the spread of resistant bacteria. The Clear Dx System (Clear Labs, San Carlos, CA) (automated method) for sequencing was recently released, using Illumina iSeq™ technology. This automated method allows for a quicker turnaround time (TAT), including less hands-on time for processing, and allowing for a smaller run size. This study was done to compare TAT and sequence quality between the MiSeq (Illumina, San Diego, CA) (manual method) and the automated Clear Dx method for microbial surveillance.

## Methods

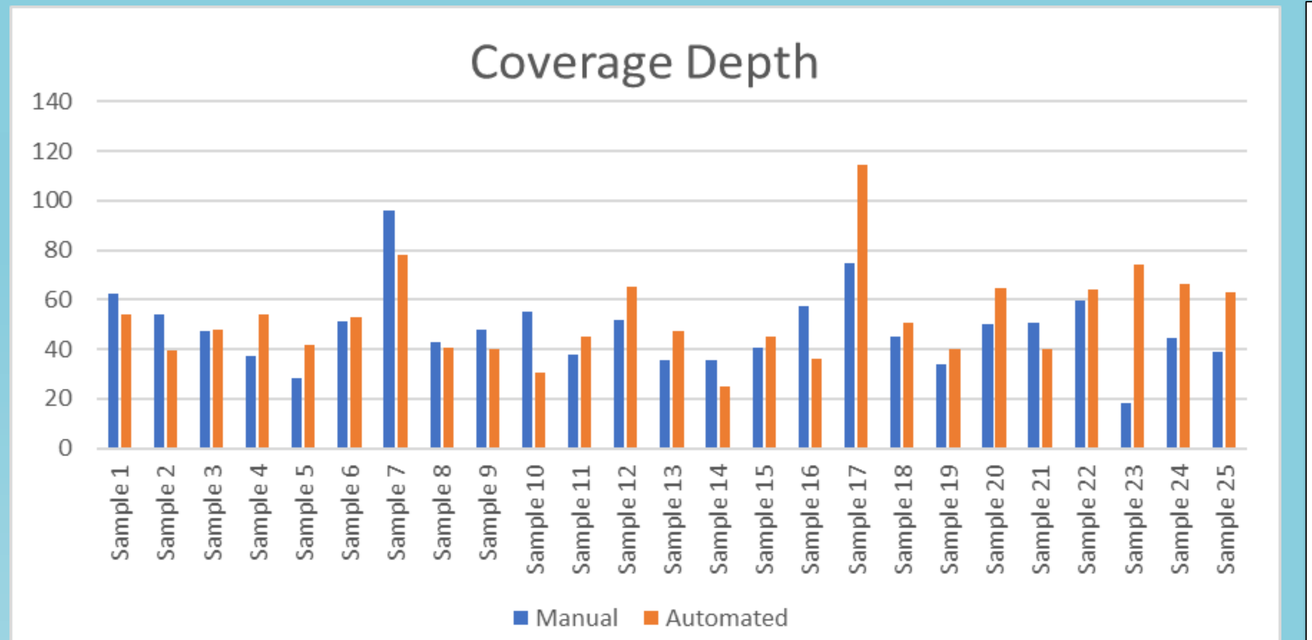
A total of 25 carbapenem resistant organisms consisting of one *Acinetobacter baumannii* (CRAB), 23 Enterobacterales (CRE), and one *Pseudomonas aeruginosa* (CRPA) were included for sequence comparison.

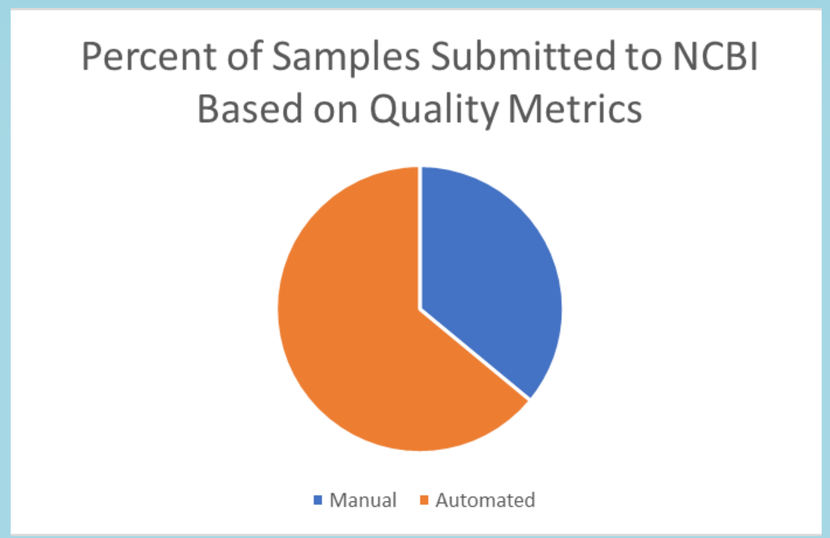
Manual Method

- DNA extracted using Qiagen EZ1 Advanced XL instrument
- dsDNA concentration determined using a Quibit fluorometer
- Whole genome sequencing (WGS) performed using Illumina DNA Prep Kit or Nextera XT Kit (500 cycle v2 kit) on a MiSeq instrument.
- Run time 48 hours

Automated Method

- One loopful of bacteria was added to 400 µL resuspension buffer in the 2 mL tube containing zirconium beads
- Samples were vortexed 30 seconds – allowed to settle for 30 seconds.
- 100 µL of supernatant was transferred to a Clear Labs sample plate.
- Sample plate, reagents, and consumables loaded onto the Clear Dx instrument.
- Run time 27 hours




## Results

- Both methods identified all samples as the same organism and MLST schemes where available.
- The assembled genome length, percent QC content, and Kraken2 genus alignment percentages were comparable between the two methods.
- Two CREs failed coverage QC using the manual method, while only one CRE failed coverage QC by the automated method.
- Variability for the two methods was seen in coverage depth. The automated system provided better coverage 64% of the time (16/25).

## Conclusion and Future Directions

- The automated method proved to be a viable alternative for microbial surveillance allowing for faster turnaround times and in some cases higher quality sequencing.
- The ability to sequence antimicrobial resistant organisms in real-time will positively impact patient care and help prevent the spread of disease.
- Future studies and research can be conducted to investigate outbreaks in medical facilities using automated sequencing.