

WHOLE GENOME INFLUENZA SURVEILLANCE IN THE US ENHANCED WITH NATIONAL INFLUENZA REFERENCE CENTERS IN COOPERATION WITH THE CDC

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Introduction

- The 3 National Influenza Reference Centers (NIRCs) were established in 2009 as a surveillance support network to the Centers for Disease Control and Prevention (CDC).
- The current 3 U.S. NIRCs are
 - Viral and Rickettsial Disease Laboratory, California Department of Public Health (Fig 1,¹)
 - Wisconsin State Laboratory of Hygiene, University of Wisconsin-Madison (Fig 1,²)
 - Wadsworth, New York State Department of Health (Fig 1,³)
- The goal of the NIRCs is to inform influenza virologic surveillance in the United States (US)
- Specimens flow through a multi-tiered system from testing at clinical and public health laboratories (PHLs) assigned to one NIRC (see map below), then to CDC
- In recent years, surveillance testing at the NIRCs has increasingly focused on next generation sequencing (NGS) for genomic analysis

Results

- Implementation of the NGS pipeline was initiated in the NIRCs during the 2014-15 influenza season
- Since then, full genome data from 8,600 influenza samples has been generated from the NIRCs, transmitted to CDC, analyzed and contributed to public databases.
- NIRC NGS summary data from the 2018-2019 influenza season is depicted in Figure 4.
- Average turn-around time from specimen receipt at the NIRC to sequence transmission to CDC, is 13 days.
- Numerous viral changes have been detected, including influenza A/H3 3C.2a and 3C.3a clade emergence (Figure 5), HA codon deletions in B/Victoria viruses, reassortants, neuraminidase variants that impacted fitness and drug resistance, and RNA polymerase analysis for assessment of new drug targets.

Figure 1. Geographic Distribution of NIRC and Representative PHLs

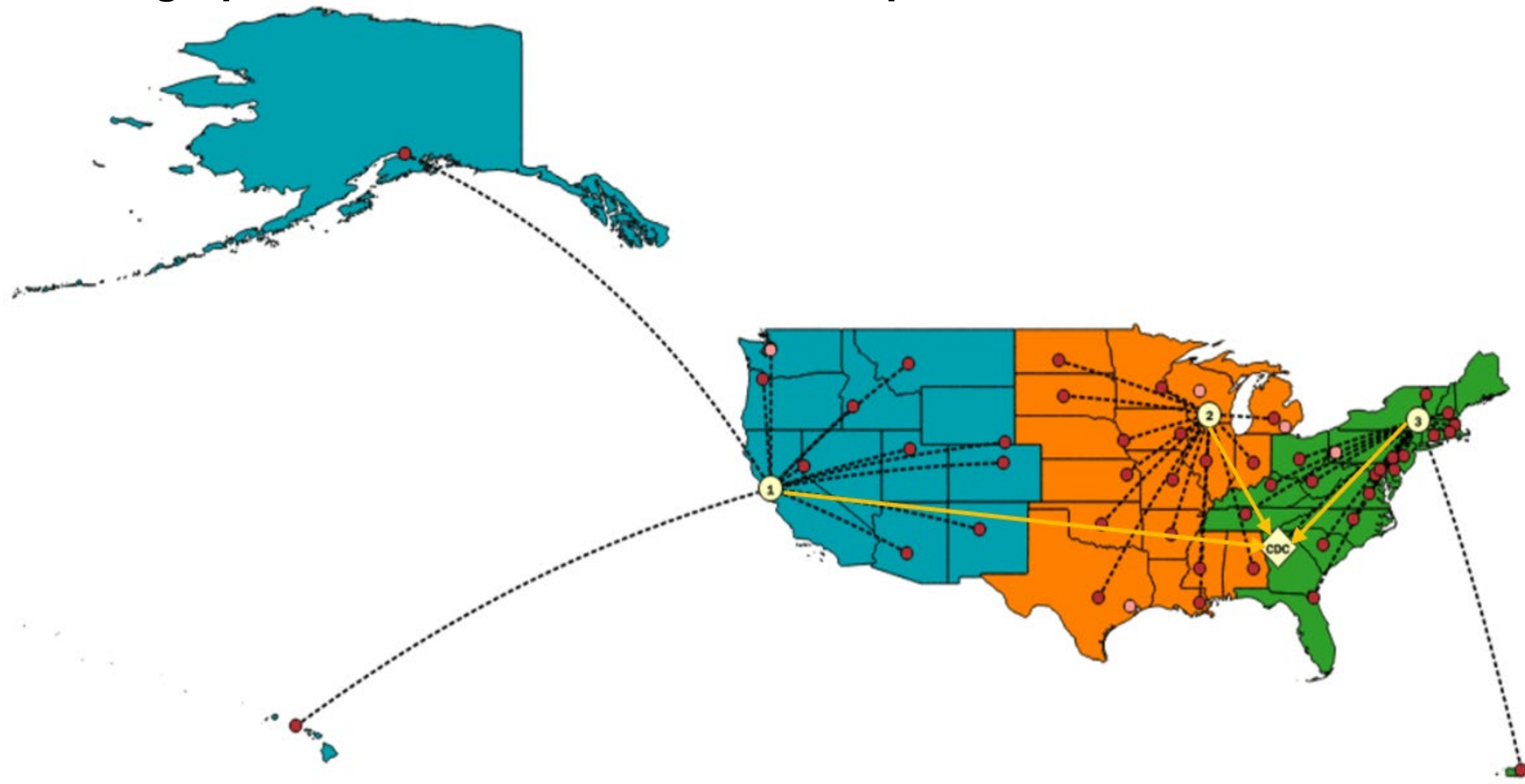
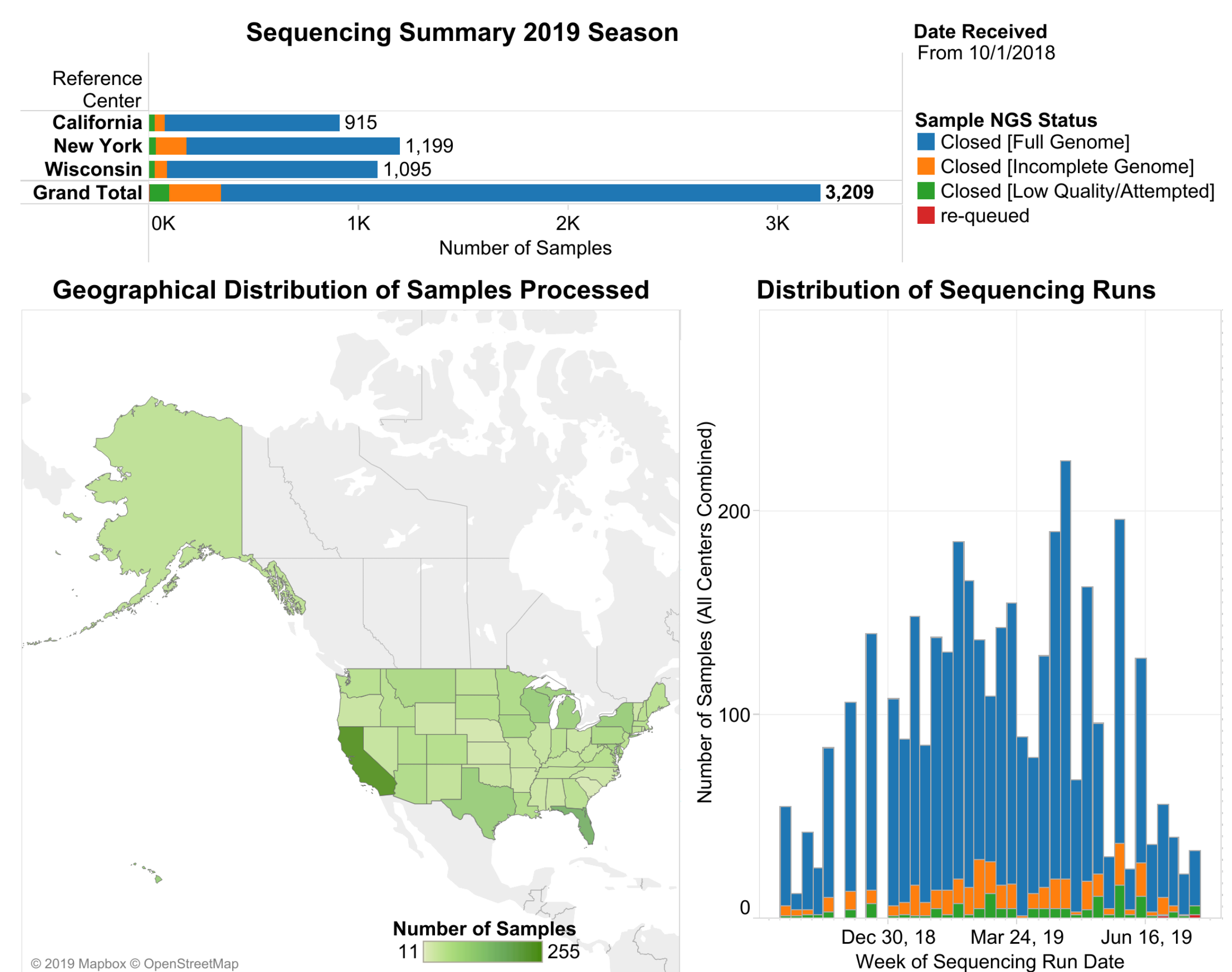


Figure 4. NIRC NGS Summary Data 2018-2019 Influenza Season



Methods

- US PHLs submit representative influenza-positive specimens to assigned NIRCs biweekly (Figure 1) according to Right Size specimen submission guidance*
- NIRC influenza specimen workflow Figure 2: Viruses are cultured and aliquots are sent to CDC for further testing
- NIRC NGS workflow Figure 3: A portion of the original specimen is used for genomic sequencing with NGS
- Sequences are analyzed and curated through an integrated genome assembly pipeline within a cloud infrastructure and transmitted through secure channels to the CDC for further analysis

Figure 5. NIRC Sequenced Specimens by Genetic Group Designation

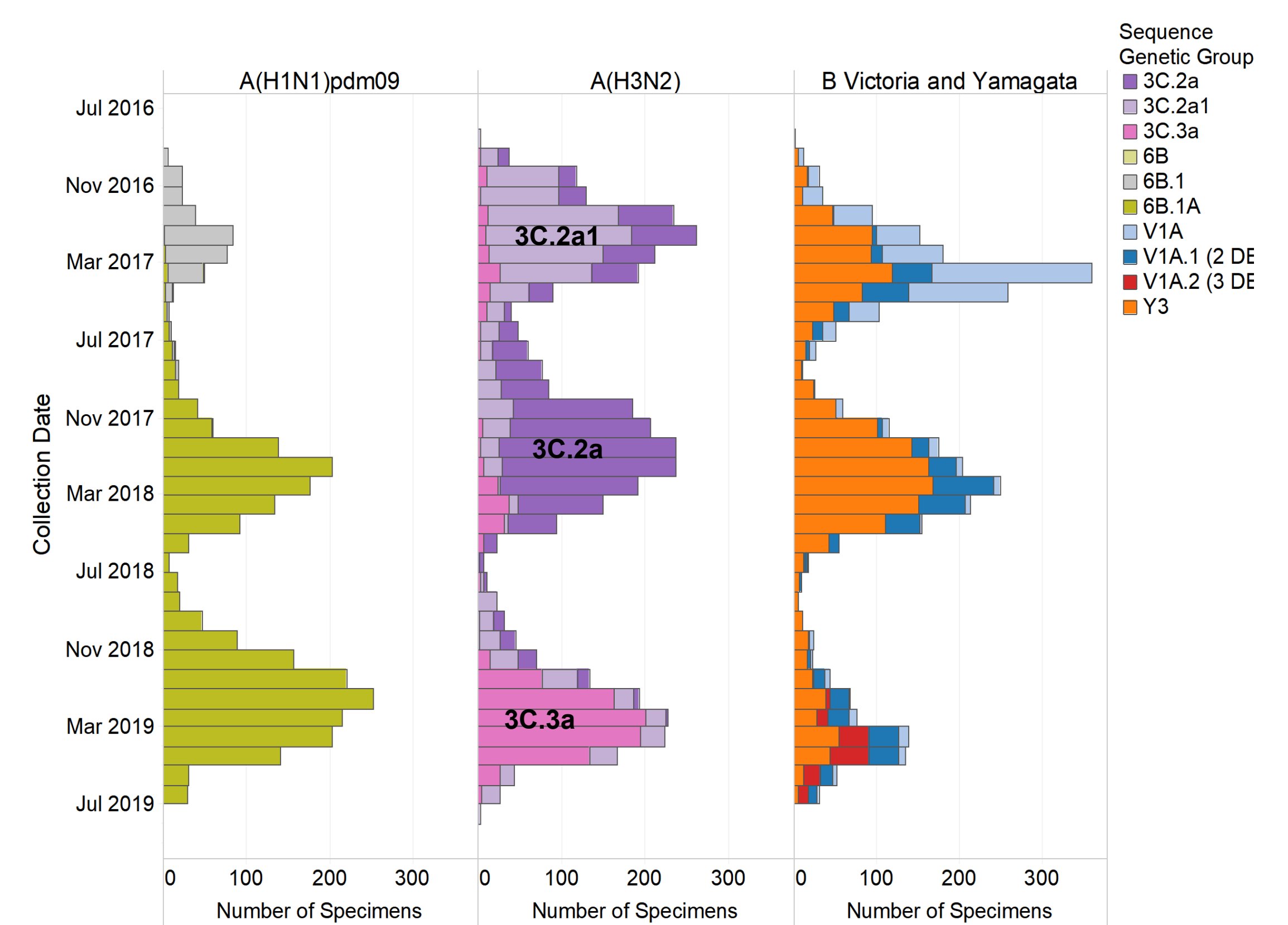


Figure 2. NIRC Influenza Specimen Workflow

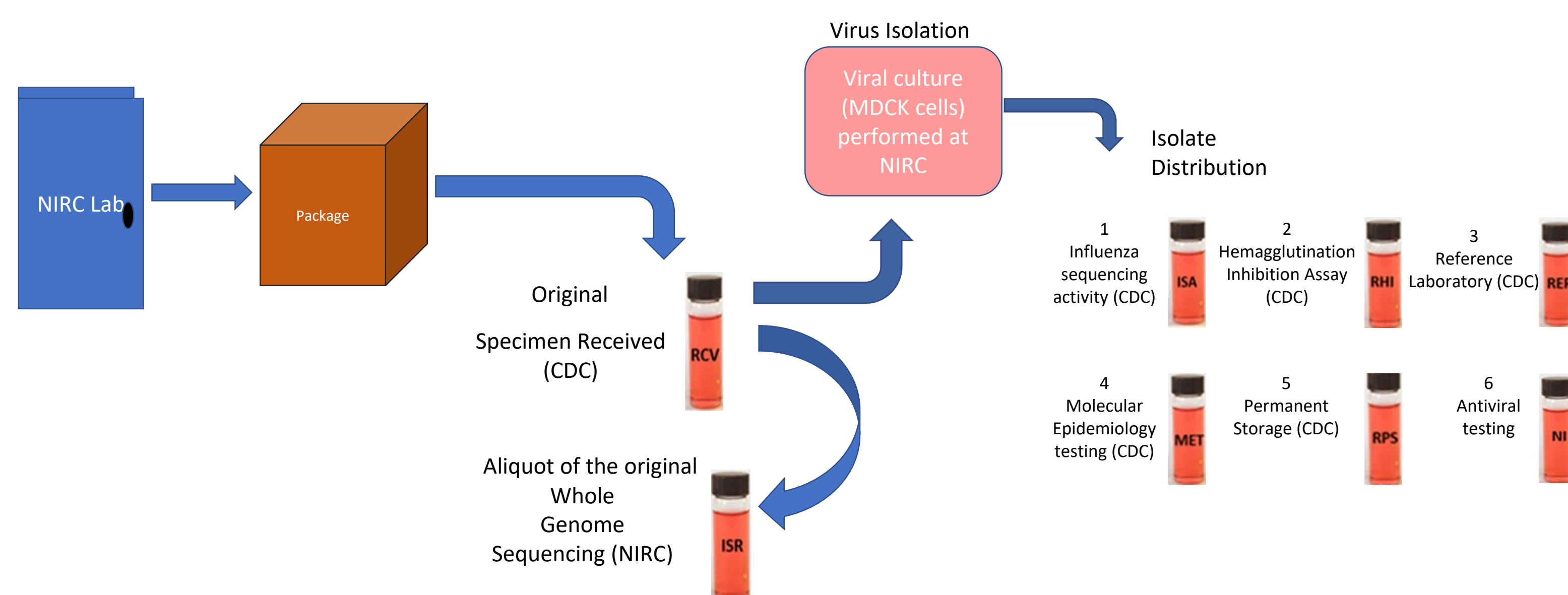
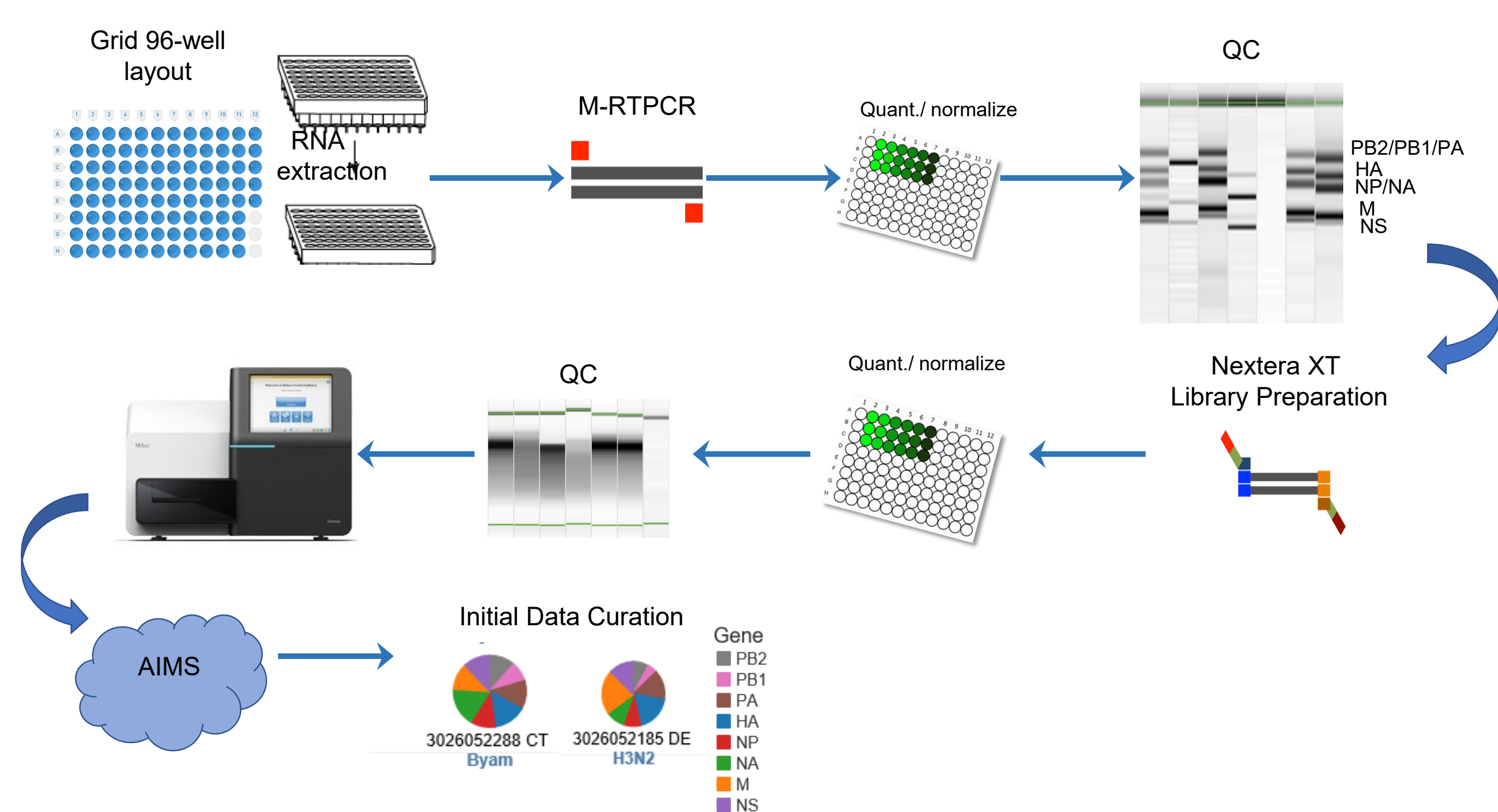


Figure 3. NIRC NGS Workflow



Conclusion

- The use of NGS facilitates the global analysis of influenza virus genomic changes in a single, high-resolution data set, enabling timely intervention strategies and improved data availability for vaccine strain selection.
- Advances in methods and platforms have enabled its application for systematic influenza surveillance and implementation at coordinated reference centers in the US, resulting in the rapid detection of evolutionary trends in circulating viruses.

Works Cited and Disclosure

* Association of Public Health Laboratories. Influenza Virologic Surveillance Right Size Roadmap.

http://www.aphl.org/AboutAPHL/publications/Documents/ID_July2013_Influenza-Virologic-Surveillance-Right-Size-Roadmap.pdf. Published July 2013.

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