

# Assuring Laboratory Quality in an Emergency

## Experiences and Lessons from Novel H1N1

Susan U. Neill, Ph.D., M.B.A.  
Director, Laboratory Services Section

- Challenges

- Volume of specimens
  - Assure quality specimens
  - Store appropriately
- Triage
  - Identify most critical
  - Sort and maintain organization
- Required additional staff
  - DSHS
  - Temporary Employees
    - Documentation of education and experience
- Training
- Equipment
- Supplies/Reagents

# APHL-CDC Laboratory Preparedness Activities

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- 28 states funded for influenza clinical outreach activities, completed fall 2008
- Influenza Molecular Diagnostic Quality Assessment Panel “CDC protocol assay” – 49 states completed March 2008
- Models used for estimating pandemic workloads, laboratory capacity, and resource requirements to aid the development of pandemic plans in 20 states over winter 08-09
- Annual 50 state PH lab calls with CDC to discuss surveillance requirements, virus changes, testing recommendations (2004-2008)
- Annual clinical lab “Influenza Update” teleconferences (APHL-NLTN)

# Seasonal Assay roll-out

- Seasonal/H5 Influenza 5 target assay
  - 2004-2008: PHL's used CDC "protocols" to establish RT-PCR testing after participation in CDC-APHL training
  - 2008: FDA compliant validation studies of 5 target assay and reagents on ABI 7500Fast completed
  - FDA cleared the CDC panel on Sept 30, 2008 with some special controls, including requirements for training of end users
  - Hands on 5 target real-time PCR assay FDA compliant training
    - 44 PHL's - April-May 2008
    - 40 PHL's April 2009 (just prior to outbreak)
  - ABI 7500Fast DX upgrades in PHL's began January 2009
    - Stringent calibration, maintenance and performance specifications
  - FDA cleared seasonal/H5 assay used in qualified labs 08/09 flu season

# Seasonal Assay Roll-out

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- Seasonal/H5 Influenza 5 target assay
  - Provides FDA cleared standardized protocol and primer/probe reagents
  - **“Qualified lab”**
    - Use of FDA cleared ABI 7500Fast with DX upgrade required
    - Participation in CDC sponsored training required
    - Completion of Performance Qualification (PQ) panel required

# Novel H1N1 Outbreak Response

- Use of seasonal FDA cleared assay in qualified labs or CDC “protocol” assay – unsubtypables sent to CDC for H1N1 (swine-like) confirmation
- EUA swine flu assay 2<sup>nd</sup> tier test (based on seasonal flu protocol) with **standardized primer-probe reagents** for universal influenza A (1<sup>st</sup> tier), universal swine, novel H1N1 deployed May 1, 2009
- Qualified labs: **ABI 7500Fast, participation in CDC sponsored training**
- **Confirmation of minimum 5 positives by CDC Influenza lab**
- Equivocals and unsubtypables referred to CDC for **ongoing QA** of assay and lab performance
- APHL-CDC outbreak and **technical assistance calls** for PHL’s beginning April 23, ongoing
- CDC detailed **“protocol training” call** for all PHL qualified and qualification eligible (obtaining requirement equipment) labs to meet FDA emergency training expectations.

# Texas LRN Influenza Labs



## Background

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- Two original cases detected in Southern California
- One of those, a 10-year-old boy, traveled to Dallas for an extended visit with relatives
- April 23 press release stated that swine flu had been confirmed by the CDC in two 16-year-old boys from Guadalupe County near San Antonio
- We received our first specimens on 4/24/09, one was reported as “Influenza A – Unable to type” on an 18-year-old boy from Guadalupe County
- Confirmed by the CDC as Swine Flu

# Background

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- Outbreak began in Mexico
- Cases quickly identified in Texas
- No understanding early in response of:
  - Severity of disease
  - Populations affected
  - How quickly the virus would spread
- Leadership requested health care practitioners submit specimens on all patients presenting with influenza like illness

## Practitioners Responded

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Day 1, April 24 <sup>th</sup>	8
Day 2, April 27 <sup>th</sup>	34
Day 3, April 28 <sup>th</sup>	530
Day 4, April 30 <sup>th</sup>	1139

## Overwhelmed

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- Front Page of Austin American Statesman on May 2, 2009
- “Flood of flu tests clogs up state lab”
- Received over 11,150 specimens total
- Requested assistance from other state laboratories, Tennessee and Virginia agreed to help with testing

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During a typical influenza season (between October and May of each year) the DSHS laboratory typically receives ...

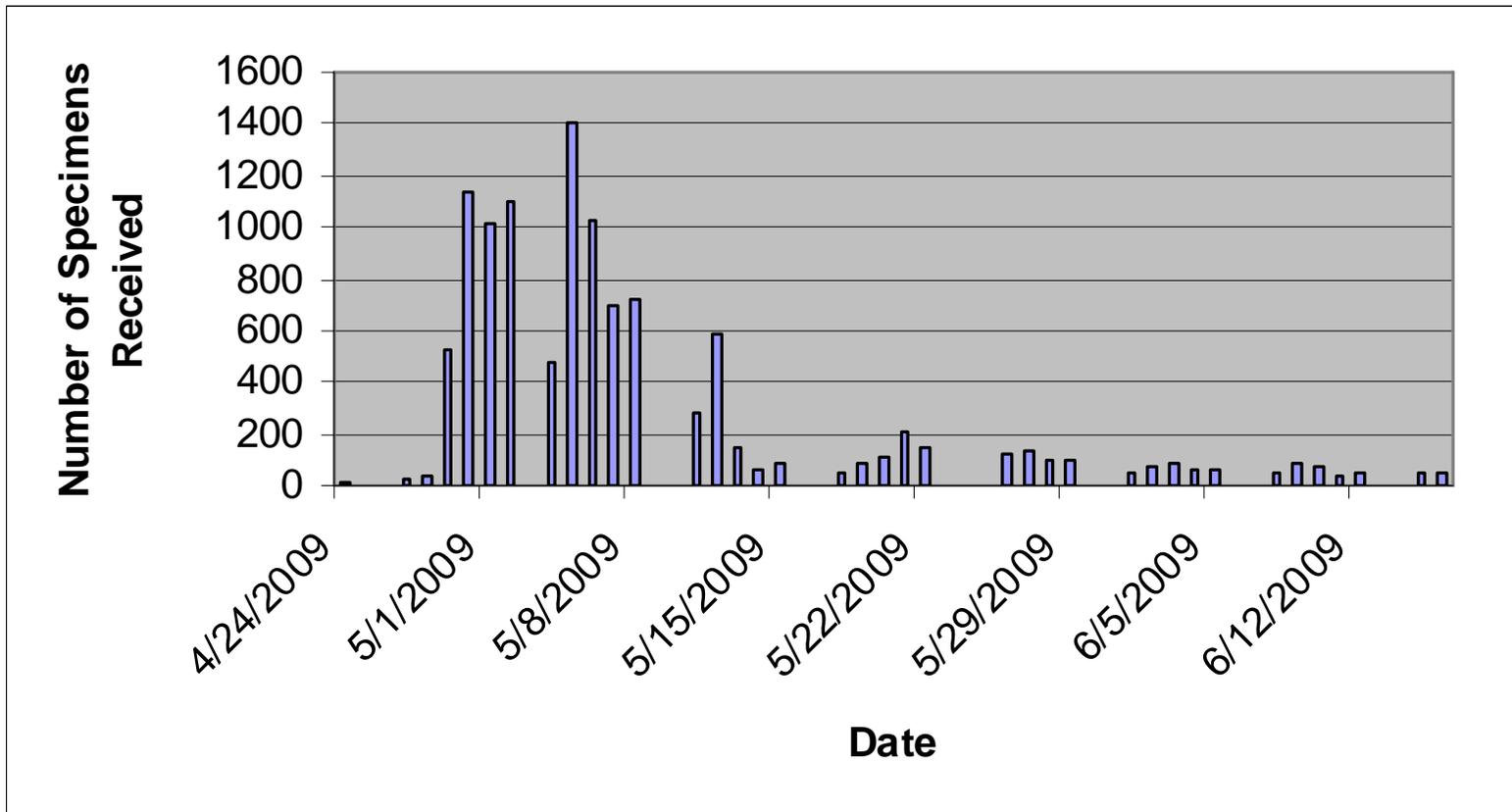
**1,500 specimens total**

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During the response to the H1N1 outbreak in Spring / Summer 2009, the DSHS laboratory received...

**1,000 to 1,500 specimens per day**

# Specimens Received



# Storage



# Staffing

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- PCR testing personnel– 2 staff originally trained
  - Identified 22 additional staff internal
  - Hired 15 temporary staff through temp agency
- Non-testing personnel
  - Specimen acquisition
  - Media Prep (VTM)
  - Shipping
  - Call Center
- QA officers
  - Screened staff background, resumes, transcripts
  - Placed in appropriate positions
  - Developed and distributed training forms
  - Assured completion of training forms as staff assumed additional duties

# Workspaces



# Testing Procedures

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- QA officer involved in all discussions of testing protocols
- Modified testing algorithm as appropriate
- Assays used
  - Seasonal influenza PCR
  - H1N1 PCR
  - Luminex RVP
- Developed a modified establishment study for assays based on panels of 20 specimens
- Used package inserts as interim SOPs
  - Interim SOPs signed by lab director

- ABI 7500 FAST DX
  - EUA of ABI 7500 FAST
  - Able to increase capacity from one to four
  - Compare results
- Luminex platform
  - Results compared with ABI 7500 FAST DX
- Extraction
  - Manual
  - MagNApure

# Equipment



## Reporting

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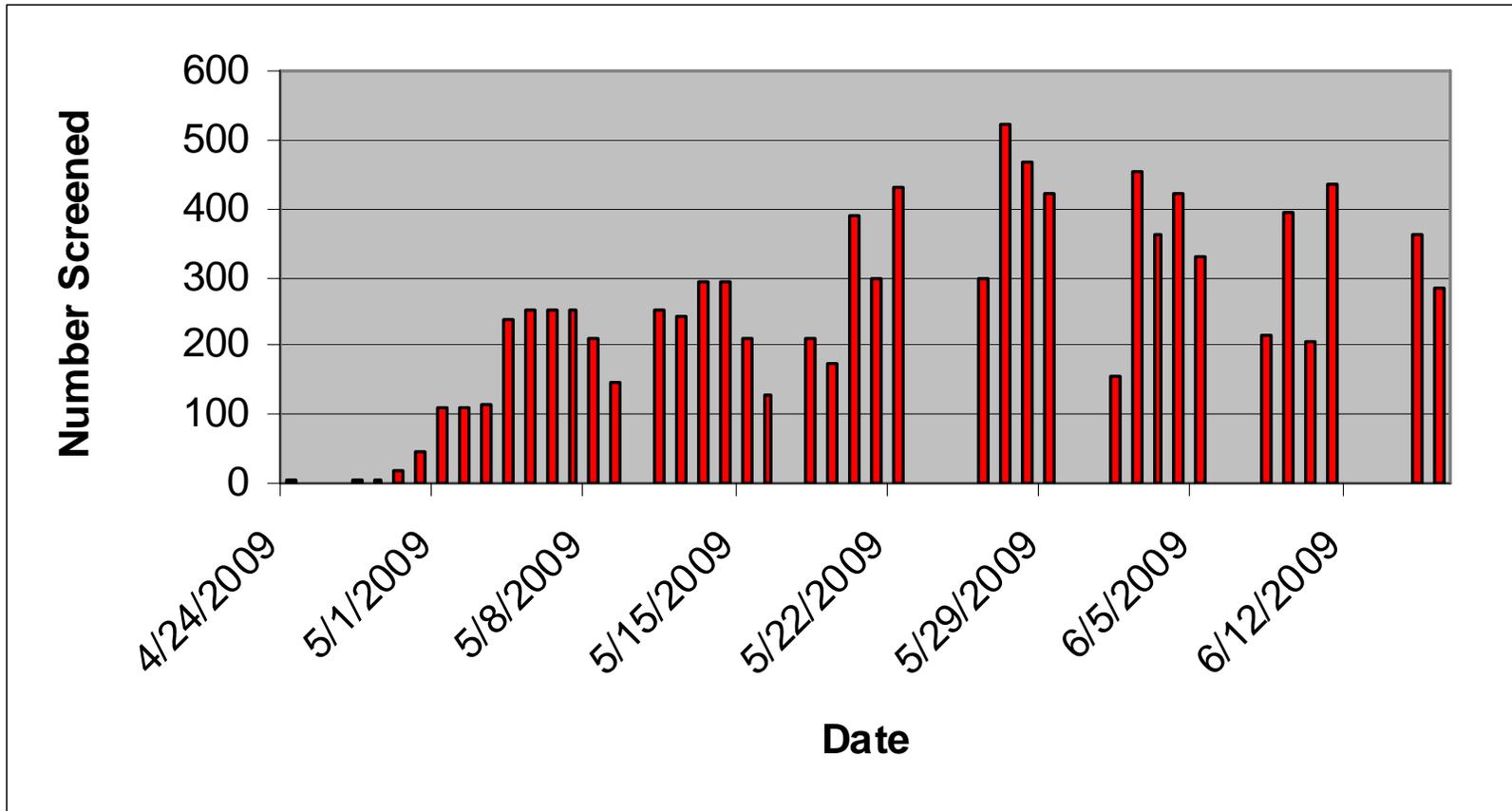
- Distributed Healthcare Provider and Patient Information Sheets required by EUA
- Modified patient reports as algorithm changed to reflect testing performed
  - No influenza detected
  - No influenza A detected
  - Influenza A, unsubtypeable
  - Influenza A, suspect novel H1N1
  - Influenza A, confirmed H1N1

# Reporting issues

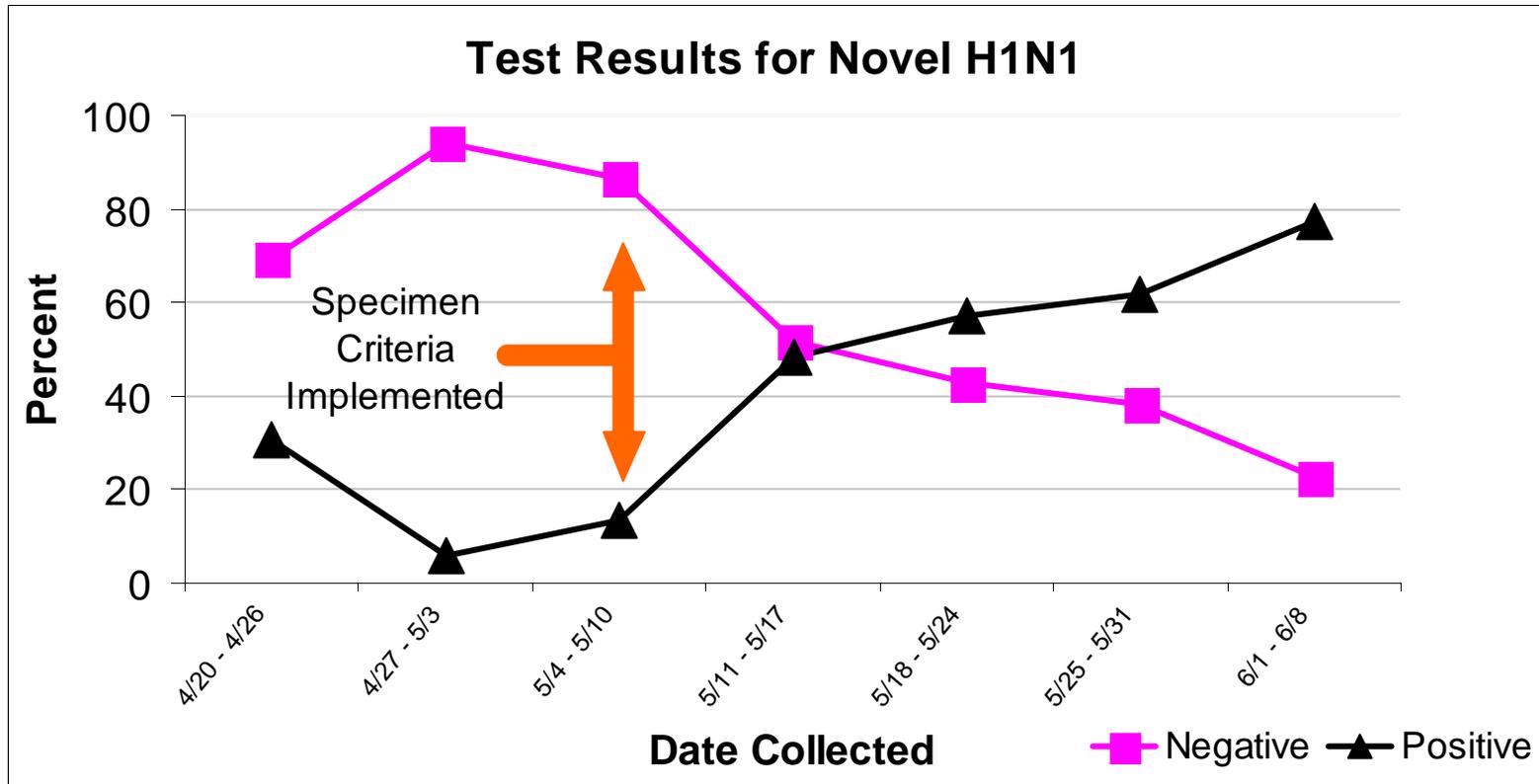
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- Testing performed by other state laboratories
  - Could not readily get data into LIMS system to report
  - One state laboratory did not include CLIA number on influenza reports
- Testing done by laboratory without CLIA certification
  - No method to reconcile
  - Eventually all specimens retested in state laboratory
- Luminex RVP
  - Results for multiple viruses
  - Only influenza result reported

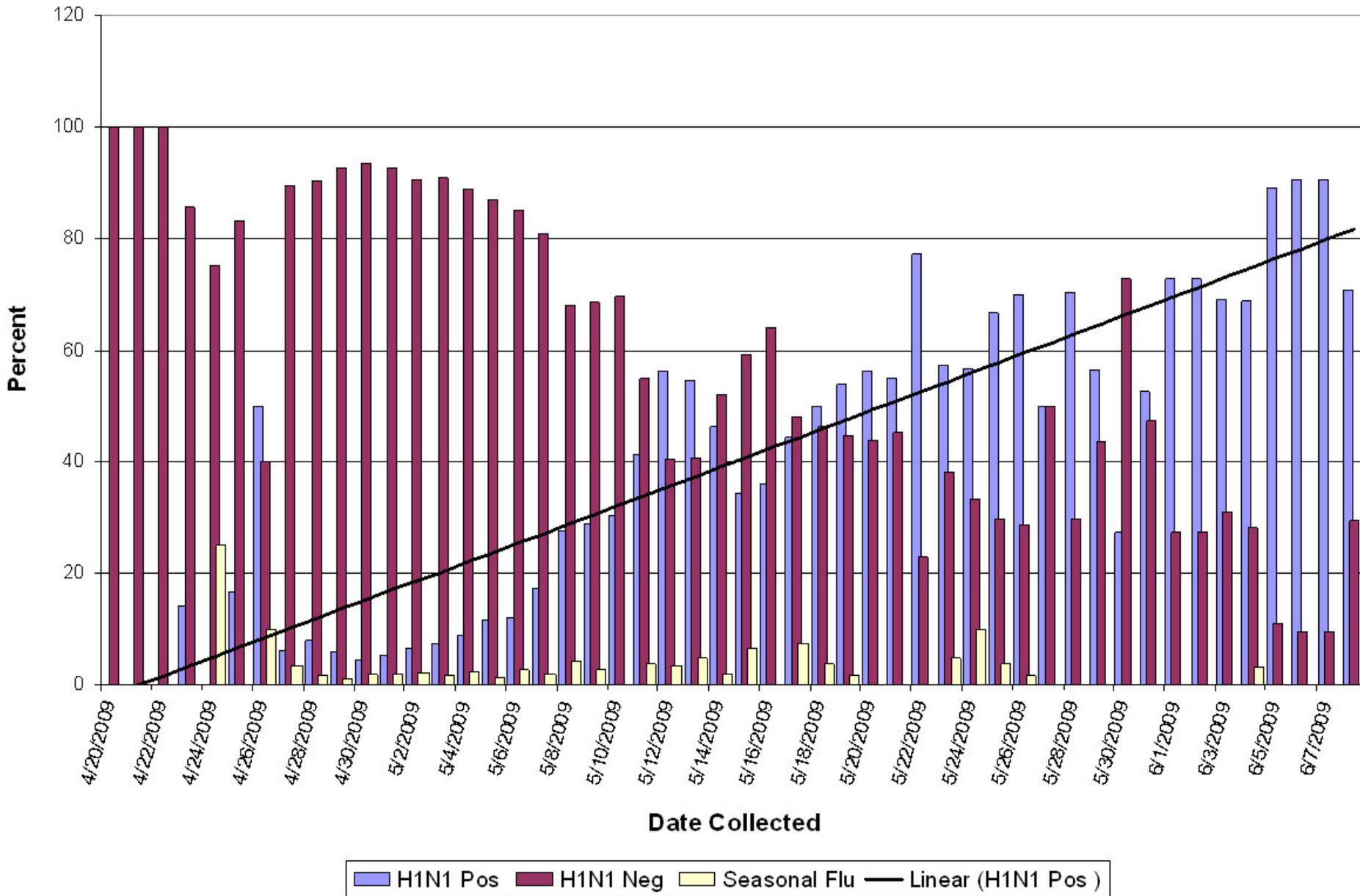
# Specimens Tested



# Effect of Implementation of Specimen Criteria



# Summary of H1N1 Analysis Since April 20th







- Identified whether a specimen was positive for novel H1N1 virus
- Did not impact treatment decisions
- Resource, time, and material intensive



- Detect novel influenza viruses
- Identify antiviral resistance
- Monitor changes in virus type

# Summer 2009 Preparations

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- Communications efforts
- Cross Training Plan
  - Internal staff identified
  - Training nearly completed
- Staffing
  - Universities
  - Temporary Agencies
- Sorting and Triage Plan
- Specimen Storage Plan
- Specimen Acquisition Plan
- Media Preparation Plan
- Testing algorithms defined
  - Workflow mapped
  - LIMs modified
- Incident Command Team