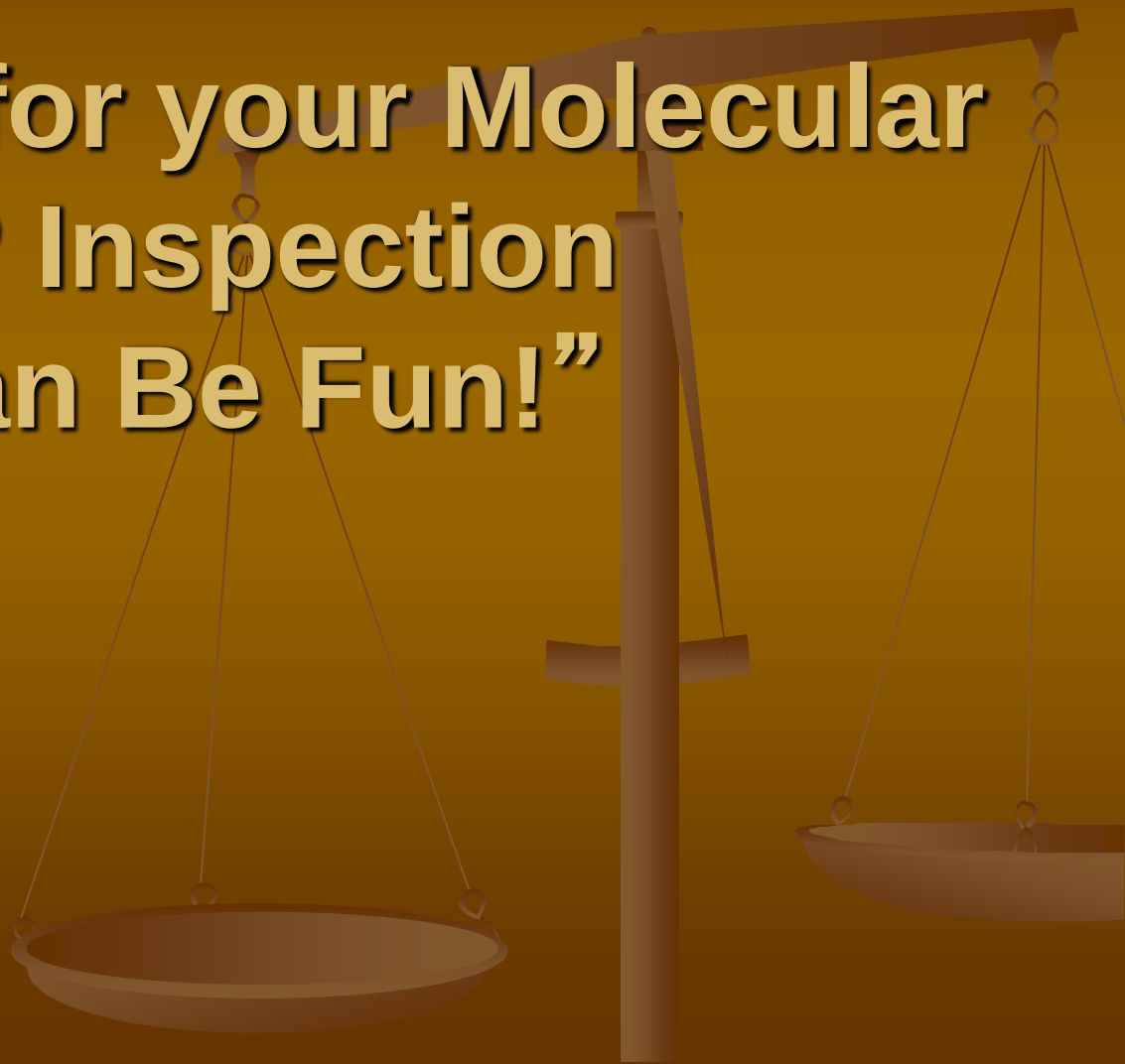
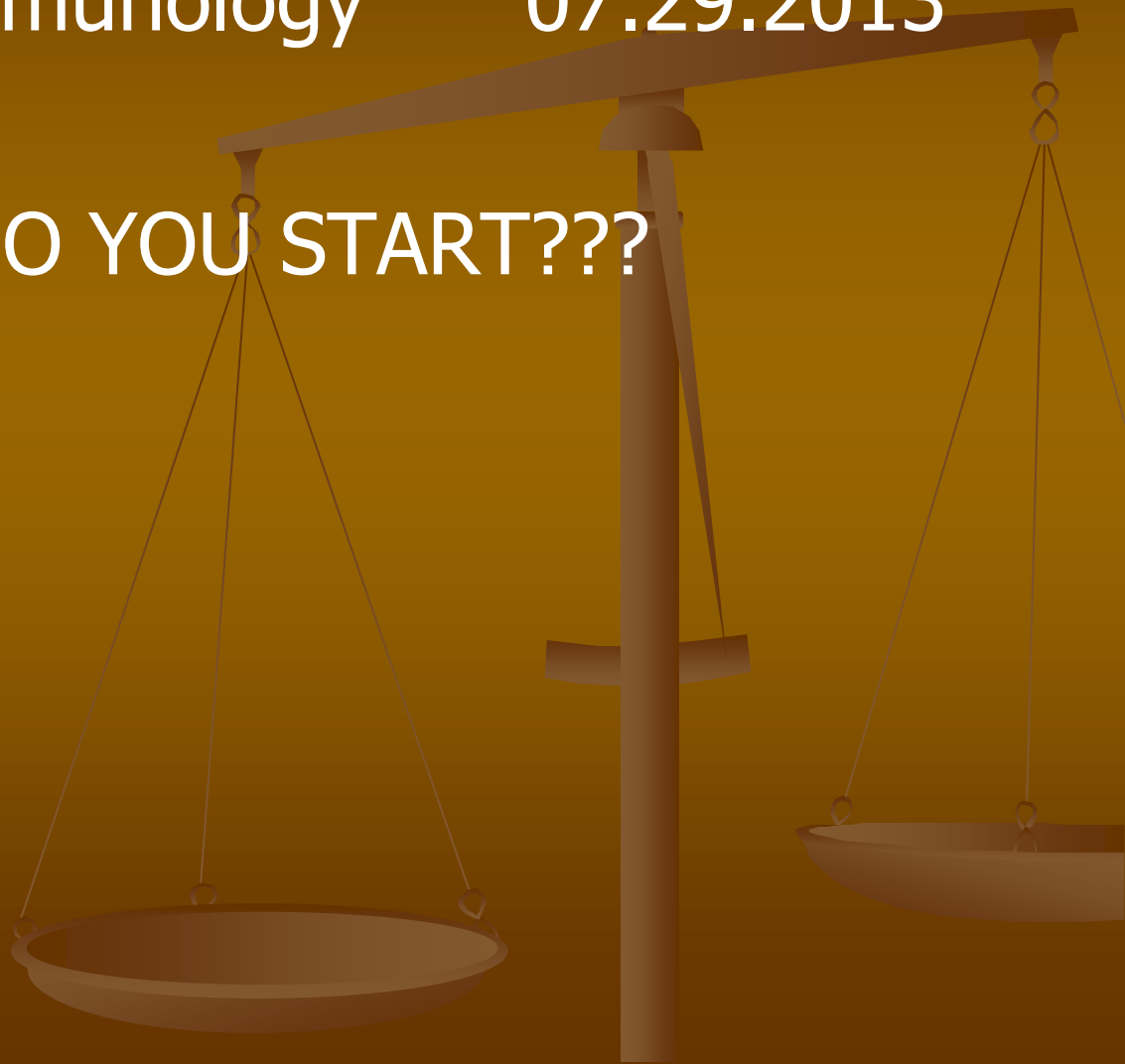
Preparing for your Molecular CAP Inspection "Can Be Fun!"



Microbiology Checklist

Microbiology/Immunology 07.29.2013

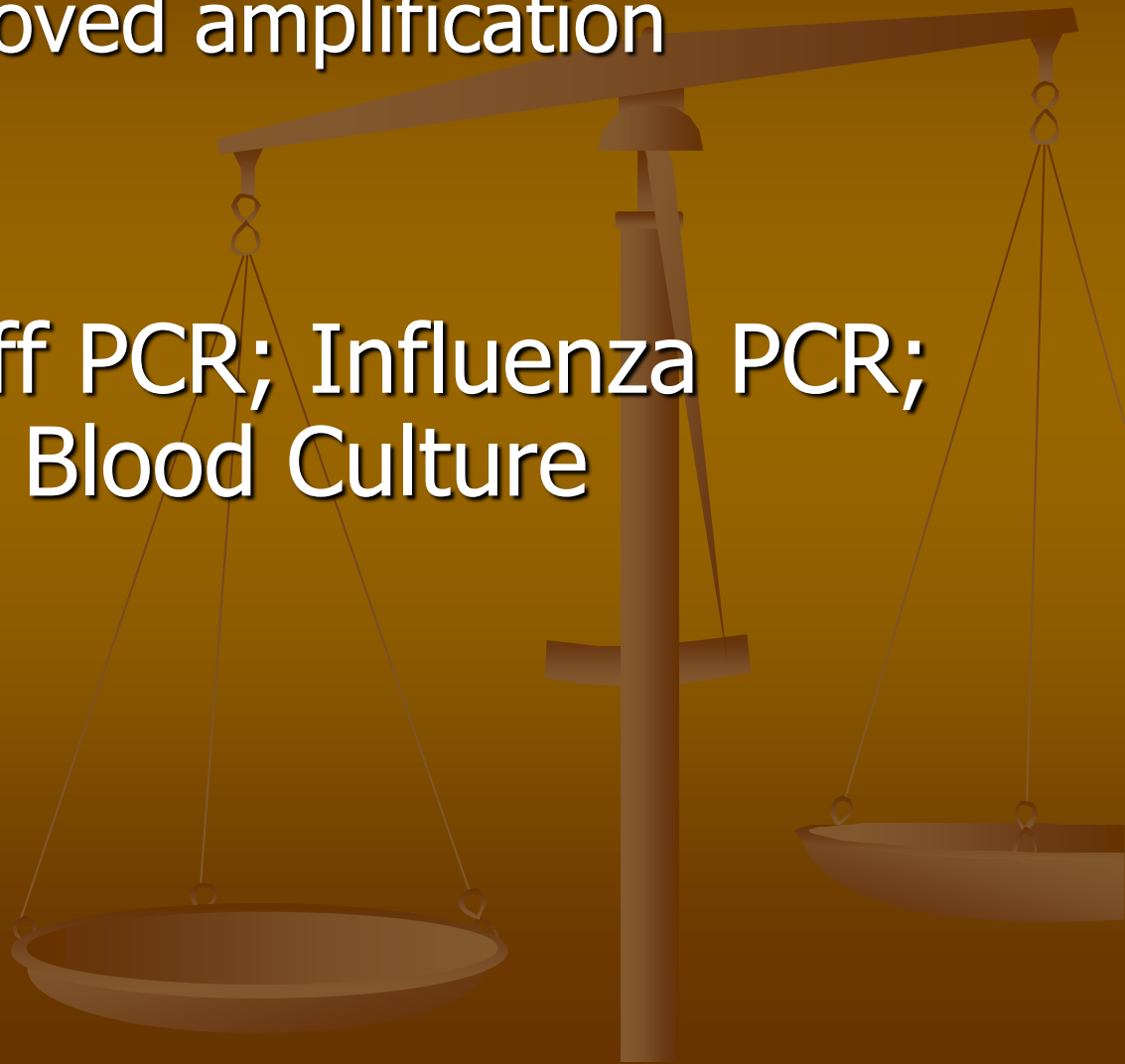
WERE DO YOU START???



Cepheid GeneXpert

FDA-cleared/approved amplification methods

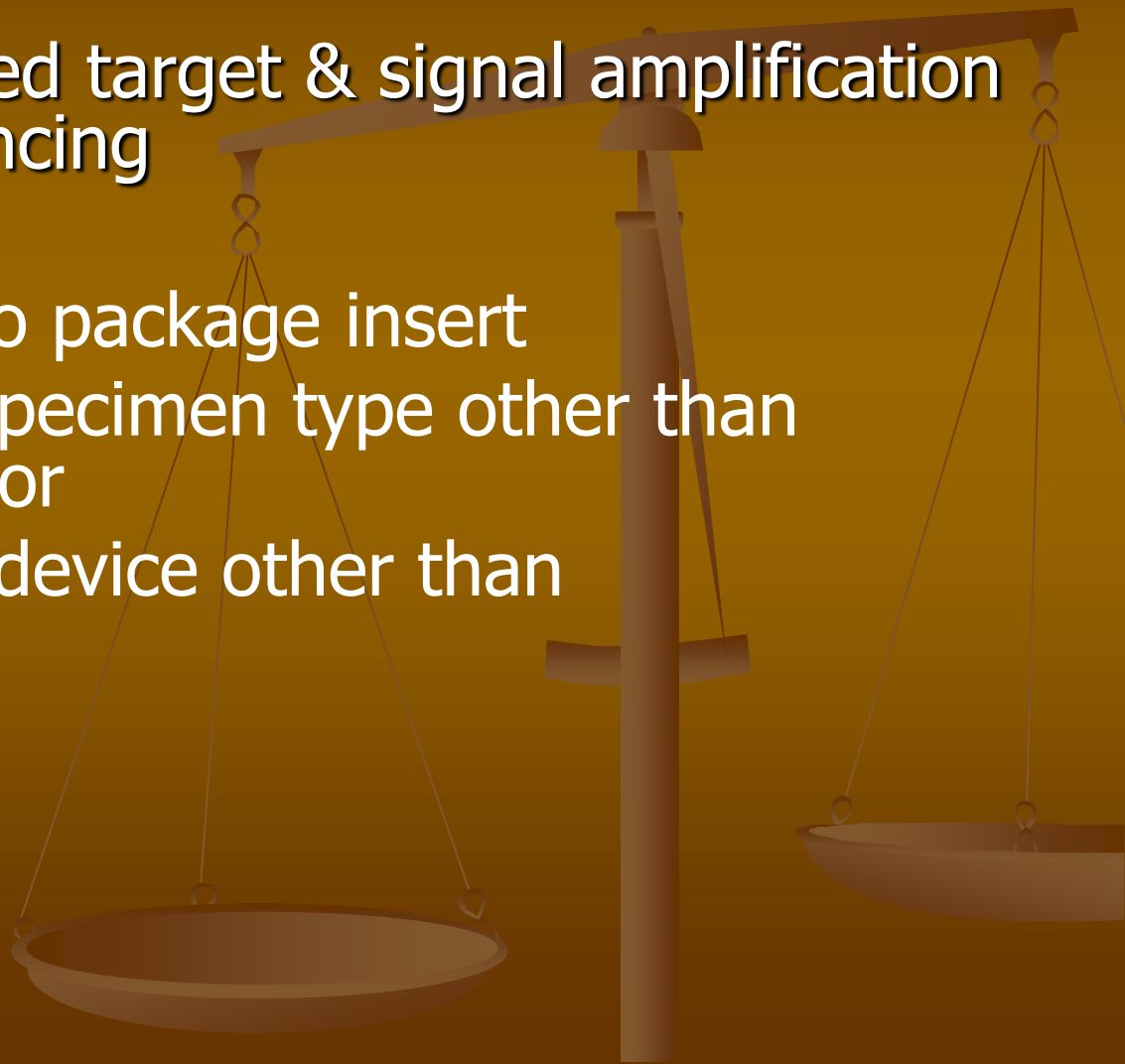
Examples: C. diff PCR; Influenza PCR; MRSA/SA PCR Blood Culture



Required Checklist Section:

FDA-cleared/approved target & signal amplification methods & sequencing

- no modifications to package insert
- using a different specimen type other than cleared/approved or
- using a collection device other than cleared/approved



QUALITY MANAGEMENT

MIC.63252 Statistics Molecular Phase I

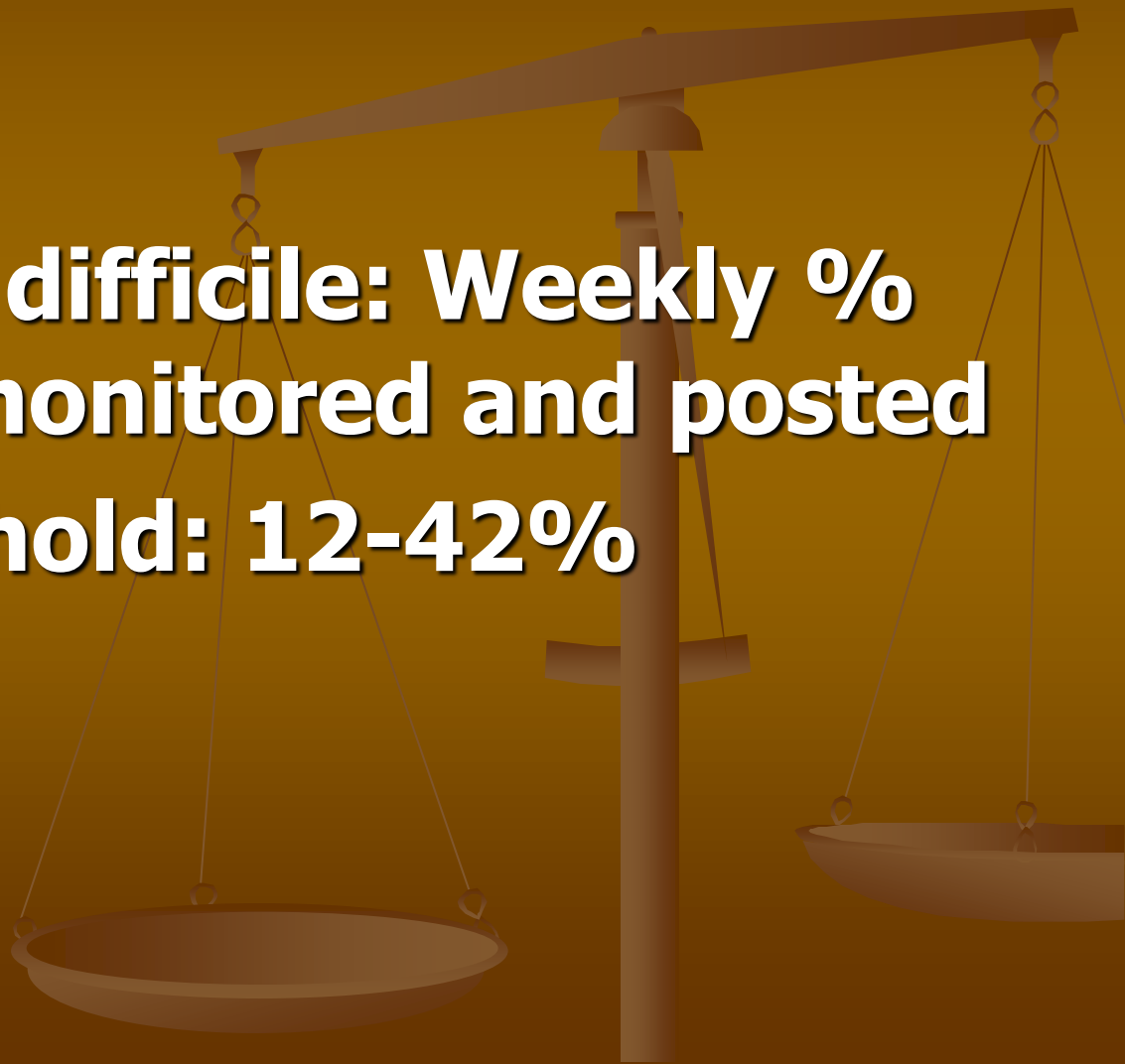
When appropriate, appropriate statistics (*e.g.* percentage of results that are positive for *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae*) are maintained and monitored.

NOTE: An increase above the expected positive rate within a run or over multiple runs should prompt investigation for potential false positive results.

Evidence of Compliance: Written procedure for calculating statistics including thresholds **AND** Records of statistical data, evaluation and corrective action if indicated

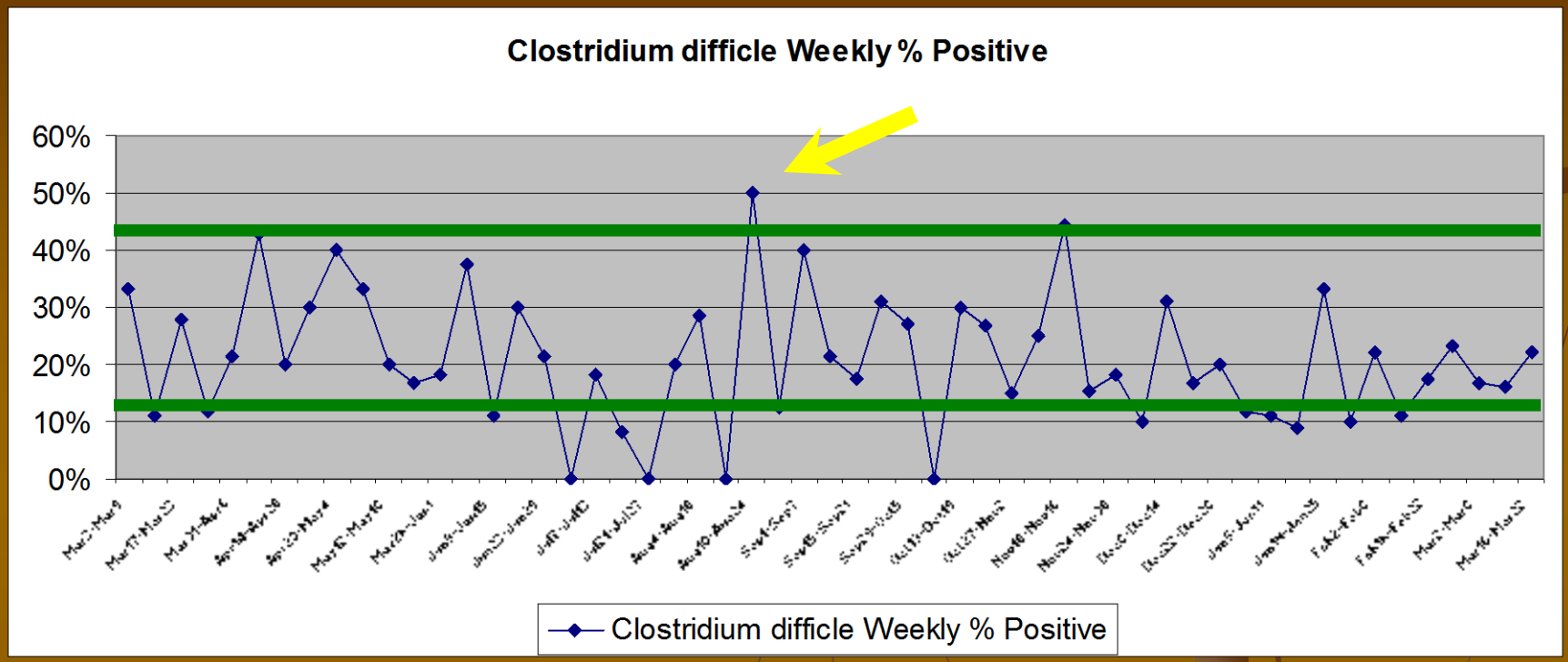
REFERENCES: CAP Master Microbiology Checklist 07.29.2013

Positive Rates MIC.63252



Clostridium difficile: Weekly % Positive is monitored and posted

Threshold: 12-42%



Aug18-Aug24 Reviewed charts and found acceptable likelihood that these are true positives based on symptoms, MD diagnosis, and previous antibiotic exposure.

Positive Rates MIC.63252

- **Xpert Flu Assay: Weekly % Positive is monitored and posted**
- **Threshold: Compared to weekly statistics supplied by the State Lab of Hygiene for Northeast Wisconsin.**
- **Evidence of Compliance:**

  Record Corrective Action in problem log of QC book. Maintain data, post graphs, and submit to the Laboratory PI committee

Influenza Positive Rates
MIC.63252

Date range		N=	% pos Influenza	P-value acceptable >=0.05	Review
Week ending	**HFM**	21	19.0%		
2/22/2014	**WSLH**	1278	12.6%	0.29	
Week ending	**HFM**	16	25.0%		
3/1/2014	**WSLH**	1151	11.2%	0.09	
Week ending	**HFM**	20	35.0%		**Nursing Home flu outbreak**
3/8/2014	**WSLH**	862	10.4%	**0.001**	
Week ending	**HFM**	13	7.7%		
3/15/2014	**WSLH**	730	6.8%	0.33	

Turnaround Times Molecular Microbiology MIC.63256

MIC.63256 Turnaround Times **Phase I**

There is evidence that the laboratory monitors sample turnaround times and that they are appropriate for the intended purpose of the test.

NOTE: There are certain clinical situation in which rapid completion is essential. An example is detection of HSV in CSF.

Evidence of Compliance:

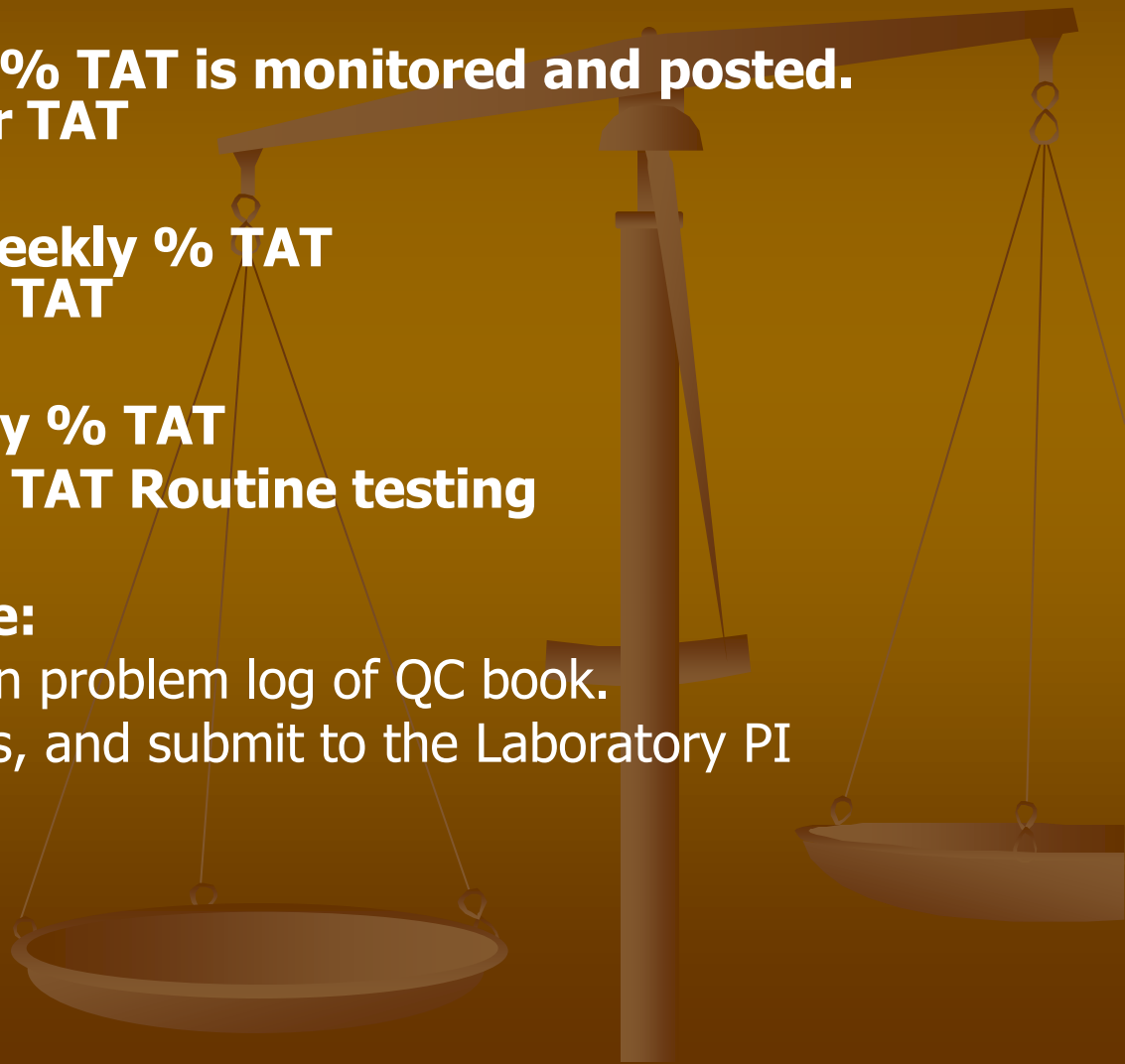
Written policy defining turnaround time and mechanism for monitoring **AND** Records showing that times defined in the policy are routinely met

REFERENCES: CAP Master Microbiology Checklist 07.29.2013

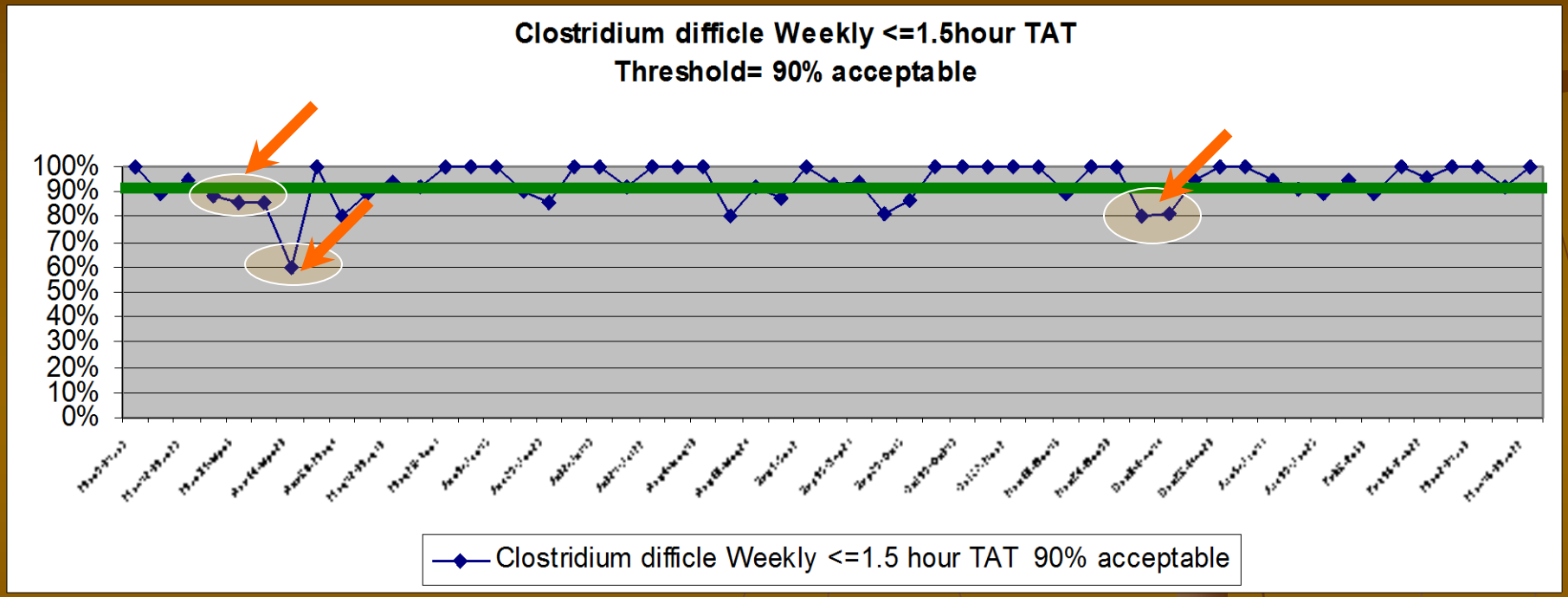
Turnaround Times MIC.63256

Microbiology monitors sample TAT for each assay.

- **BCMRSA/SA: Monthly % TAT is monitored and posted. Threshold: <=2.5 hour TAT**
- **Clostridium difficile: Weekly % TAT Threshold: <=1.5 hour TAT**
- **Xpert Flu Assay: Weekly % TAT Threshold: <=2.0 hour TAT Routine testing**
- **Evidence of Compliance:**
  Record Corrective Action in problem log of QC book.
  Maintain data, post graphs, and submit to the Laboratory PI committee.



Clostridium difficile: Weekly % TAT

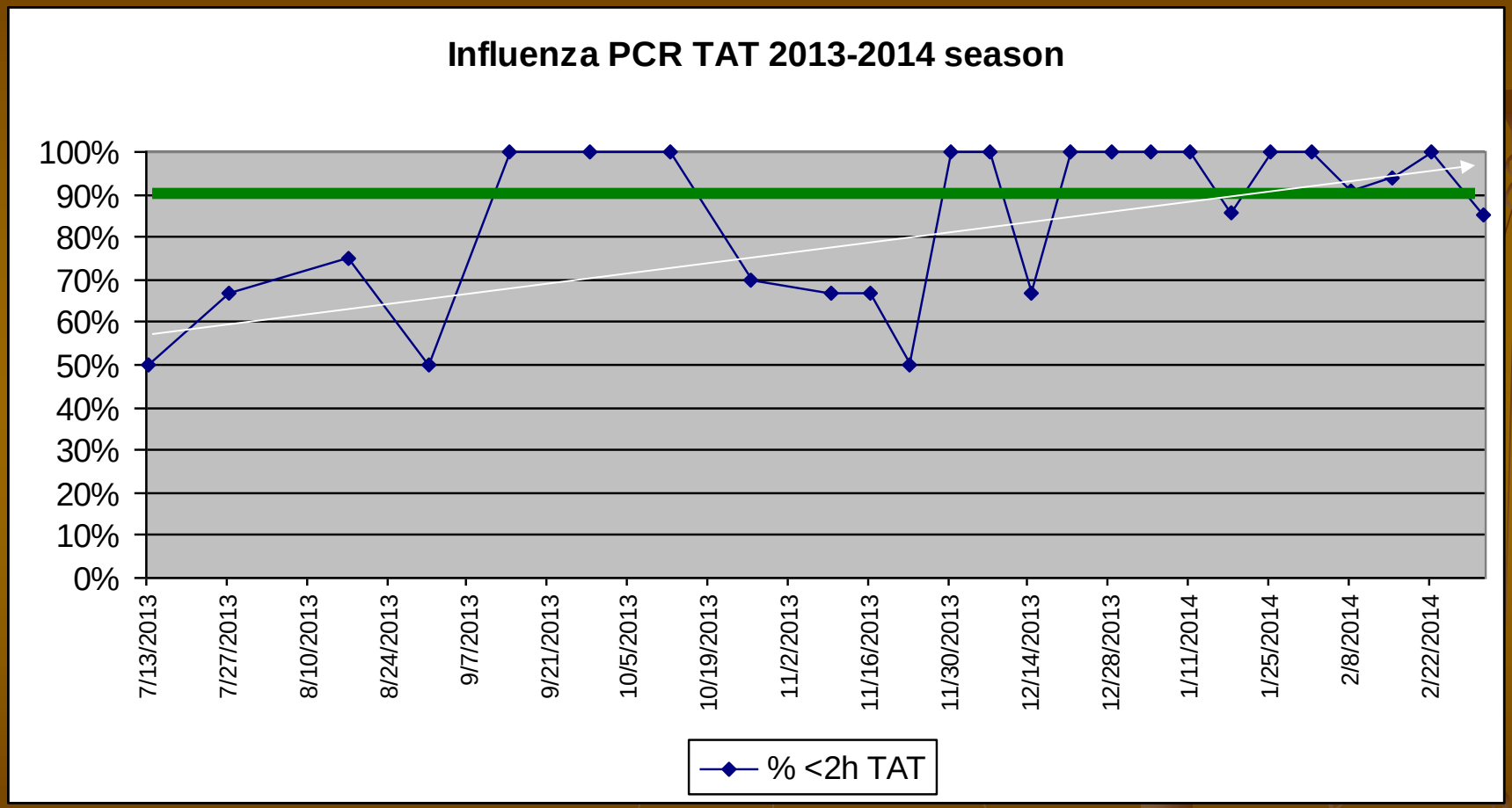


Mar 2013 Automated resulting from the interface is in place…there was some confusion with second shift regarding this which made the TATs a little longer. Will monitor over the next few weeks.

Apr14-Apr20: testing was low in numbers…continue to monitor

Dec8-Dec14: One patient had PCR inhibitors that had to be repeated without success. She also had multiple recollections. This extended the TAT due to this reason.

Influenza PCR: Weekly % TAT



Discussed with Staff the need to improve TAT

QUALITY CONTROL

MIC.63262 Daily QC **Phase II**

Controls are run daily for quantitative and qualitative tests.

Except for tests meeting the criteria in Note 3, below, external surrogate sample controls must be run as follows:*

- *For quantitative molecular tests, 3 controls must be run daily - a negative control, a low-positive control and a high-positive control, except where a specific exception is given in this checklist*
- *For qualitative tests, a positive and negative control must be run daily*

REFERENCES: CAP Master Microbiology Checklist 07.29.2013

NOTE 3: Daily controls may be limited to electronic/procedural/built -in (e.g. internal, including built-in liquid) controls for tests meeting the following criteria:

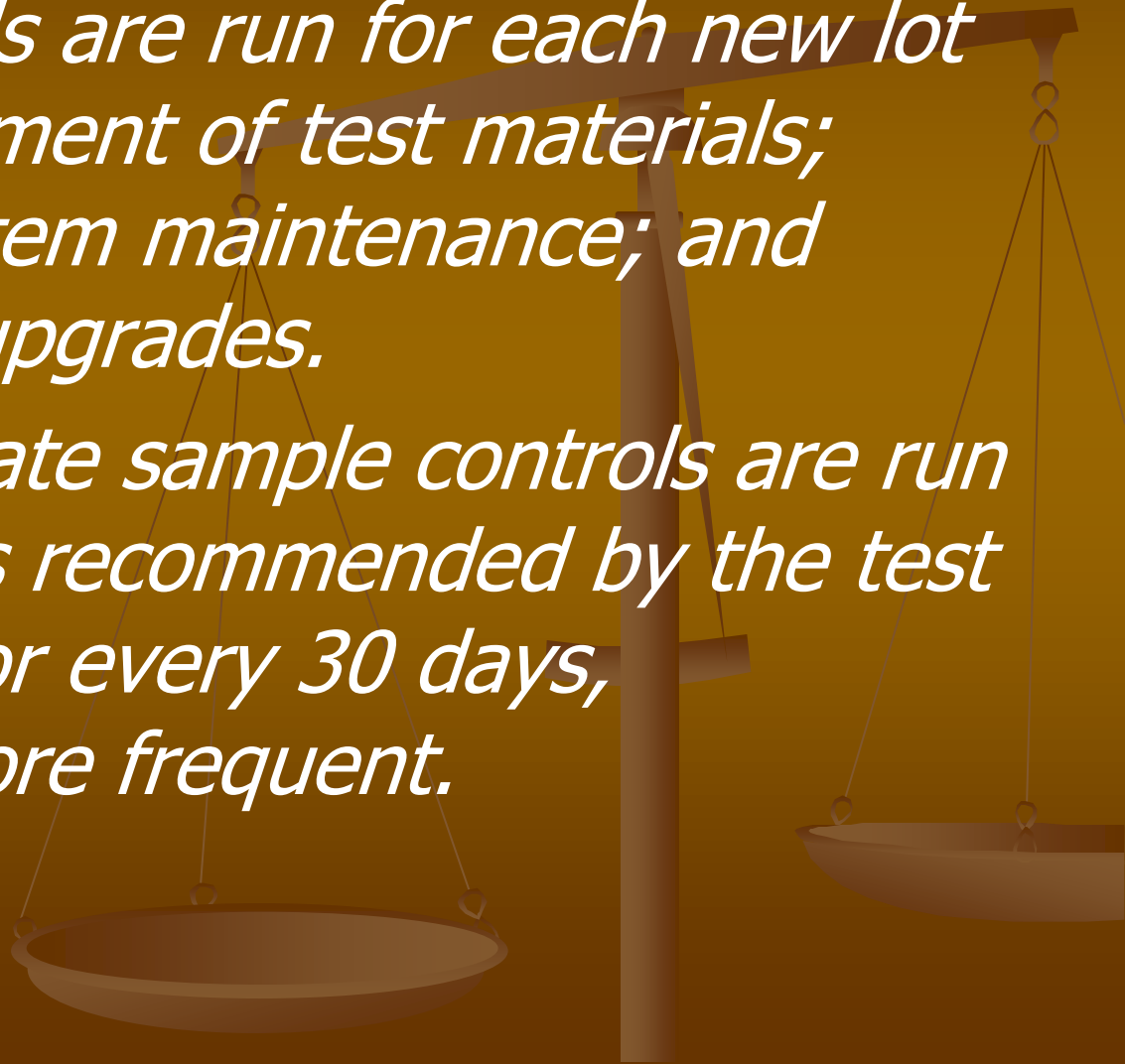
- *For quantitative tests, the test system includes 2 levels of electronic/procedural/built-in internal controls that are run daily*
- *For qualitative tests, the test system includes an electronic/procedural /built-in internal control run daily*
- *The system is FDA-cleared or approved, and not modified by the laboratory*

More on “NOTE 3”

- *The laboratory has performed studies to check the adequacy of limiting daily QC to the electronic/procedural/built-in controls. Studies must include daily comparison of external controls to built-in controls for at least 20 consecutive days when patient samples are tested.*
- *Records must be retained while an instrument/method is in service, and for two years afterwards.*
- *Corrective action must be taken if either the internal or external control is out of acceptable range during or after the evaluation process. Repeating controls or re-evaluation of the internal control system may be necessary to achieve acceptable results.*

More on “NOTE 3”

- *External controls are run for each new lot number or shipment of test materials; after major system maintenance; and after software upgrades.*
- *External surrogate sample controls are run as frequently as recommended by the test manufacturer, or every 30 days, whichever is more frequent.*



Multiplex QC

MIC.63264 *Multiplex QC* **Phase II**

- **For multiplex tests, controls for each analyte are either included in each run or rotated so that all analytes are tested periodically.**

  Evidence of Compliance:

  Written procedure defining multiplex test QC **AND** Records of multiplex test QC

- i.e. BCMRSA/SA C1 pos and C2 pos may be rotated each month as part of the external surrogate sample controls that are run every 30 days.

REFERENCES: CAP Master Microbiology Checklist 07.29.2013

Multiplex QC

MIC.63580 *New Reagent Lot - Multiplex* **Phase II**

For multiplex tests, all analytes detected by the assay are individually verified for each new shipment and/or lot.

NOTE: Verification of new shipments and/or lots may be difficult for rare organisms or subtypes. In these situations, verification may be performed annually.

Evidence of Compliance: Written procedure for new lot/shipment verification of all analytes detected by each multiplex assay **AND** Records of new lot/shipment verification

REFERENCES: CAP Master Microbiology Checklist 07.29.2013

Some of the easier ones…

MIC.63274 QC Confirmation of Accuracy Phase II

Results of controls are reviewed for acceptability prior to reporting patient results.

NOTE: Conditions causing unacceptable control results must be investigated and corrective action must be documented.

Evidence of Compliance: Written policy/procedure stating that controls are reviewed and acceptable prior to reporting patient results **AND** Evidence of corrective action taken when QC results are not acceptable

REFERENCES: CAP Master Microbiology Checklist 07.29.2013

Some of the easier ones…

MIC.63275 QC Acceptability Limits Phase II

Acceptability limits are defined for all control procedures, control materials, and standards.

MIC.63276 QC Corrective Action Phase II

There is documentation of corrective action when control results exceed defined acceptability limits.

REFERENCES: CAP Master Microbiology Checklist 07.29.2013

Quantitative assays

MIC.63277 QC Statistic Phase I
For quantitative assays, quality control statistics are performed monthly to define analytic imprecision and to monitor trends over time.

NOTE: The laboratory must use statistical methods such as calculating SD and CV monthly to evaluate variance in numeric QC data.

Evidence of Compliance: Written procedure for monitoring of analytic imprecision including statistical analysis of data

REFERENCES: CAP Master Microbiology Checklist 07.29.2013

Processes to ensure specimen integrity

MIC.63318, MIC.63322, MIC63324 are essentially dealing with specimen contamination.

- **If you are doing other lab tests on the sample, aliquots must be taken first for PCR testing.**
- **If aliquoting of specimens is performed, there is a written procedure to prevent any possible cross-contamination of the aliquot containers.**

  NOTE: Although in some cases it may be appropriate to aliquot a specimen, the laboratory must have a policy that no aliquot is ever returned to the original container.

- ***If residual samples are used for amplification-based testing, policies and procedures ensure absence of cross-contamination of samples.***

REFERENCES: CAP Master Microbiology Checklist 07.29.2013

Validation Studies - Sample Type/Collection

*****REVISED**** ***07/29/2013*** **Phase II**

MIC.64815

MIC.64770 Validation Studies - Sample Type/Collection

If the laboratory tests sample types or uses collection devices other than those listed in the package insert, the laboratory performs validation studies to document adequate performance of the test.

NOTE: Results from tests performed on sample types not listed in the package insert may be reported without complete validation only if the sample type is encountered rarely, precluding an adequate number for validation studies. Under these circumstances, the test report must include a disclaimer stating that the sample type has not been validated

REFERENCES: CAP Master Microbiology Checklist 07.29.2013

Validation/Verification Study

MIC.64860 Validation/Verification Molecular **Phase II**

There is documentation that the laboratory has performed a validation/verification study prior to reporting patient results.

- *Verify performance characteristics of the test as outlined in the package insert for all testable specimen types*
- ***Qualitative tests:*** *comparison of positive and negative test results to a comparable test method.*
  Acceptable specimens: *external control material, cultured organisms and proficiency testing material, and must include positive and negative patient samples.*
- ***Quantitative tests:*** *the manufacturer's limit of detection, linearity, reportable range, and precision should be validated/verified, as well as a comparison of patient test results across the reportable range of the test.*
  Acceptable specimens: *quantitative external control material, cultured organisms (quantified) and proficiency testing material, and must include patient samples.*

REFERENCES: CAP Master Microbiology Checklist 07.29.2013

Validation/Verification Study

Clostridium difficile RT-PCR Assay **100% correlation with expected results and Internal QC**	25 known external sample controls were run by five technologists over a period of 10 days. **ATCC strains used:** **C. sordelli ATCC9714** **C. difficile toxigenic strain ATCC 9689** **C. difficile non-toxigenic strain ATCC 700057**
Validation of Gene Xpert using 20 patient specimens were compared to a Gene Expert at Bellin and with our current EIA procedure.	**PCR vs PCR referred 100% correlation** **PCR vs EIA** **PCR detected 6 positive Patients while the EIA procedure detected 3. This is what was expected as the Xpert C difficile Assay is at least 50% more sensitive as stated in the literature and in the Manufacturers package insert.**

Validation/Verification Study

Xpert Flu A,B,Flu A 2009 H1N1 RT-PCR Assay 100% correlation with expected results and Internal QC	25 known external sample controls were run by five technologists over a period of 9 days.
	Viral strains used: *Influenza A/Brisbane/59/07(H1)* *Influenza A/NY/02/2009 H1N1* *Coxsackie virus A9*

Xpert Flu A,B,Flu A 2009 H1N1 RT-PCR Assay

Validation of Gene Xpert using 20 known simulated patient specimens was performed.

- ***100% correlation was seen with the expected results of this validation panel***

Simulated patient specimen viral strains used.

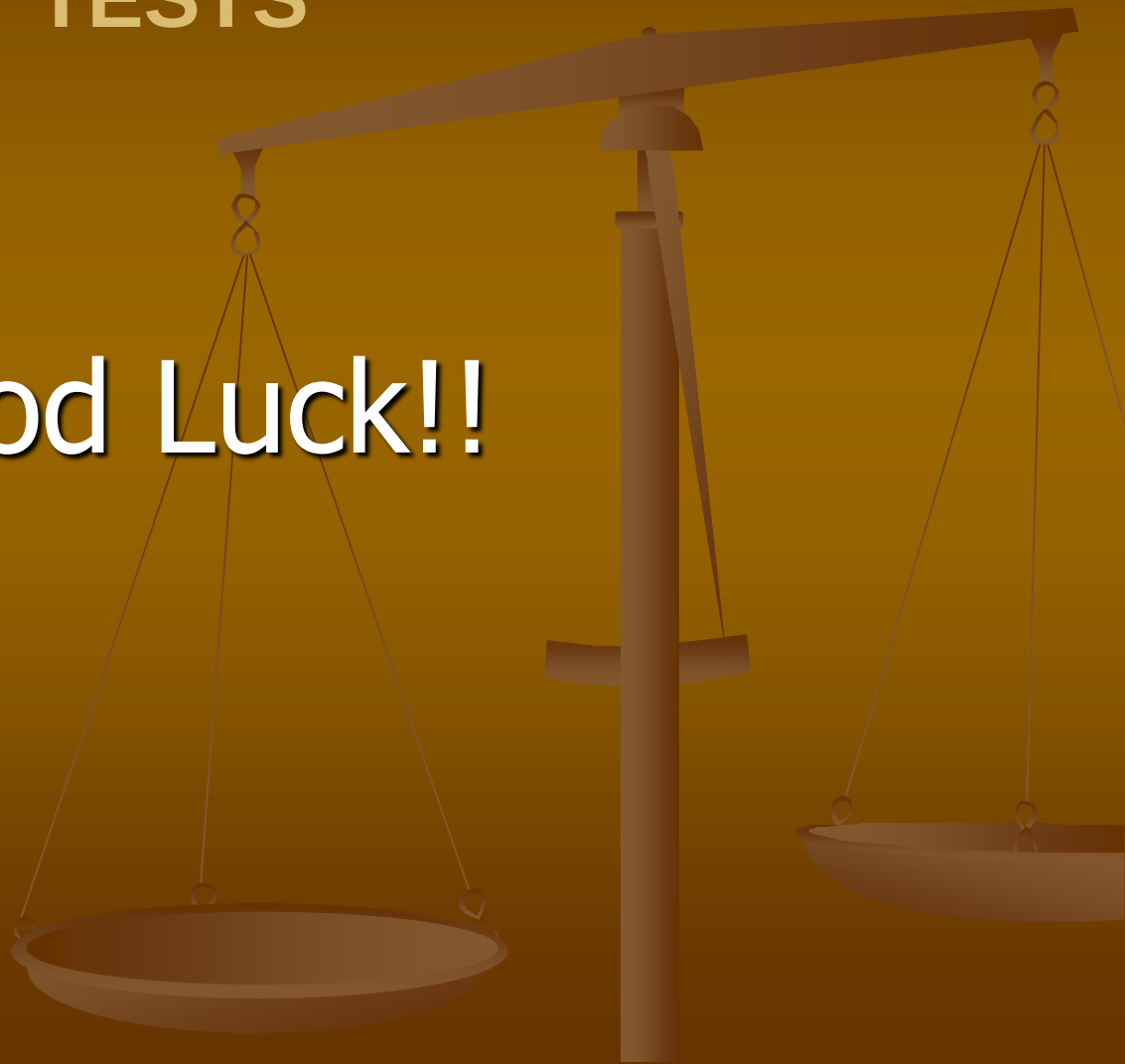
X2 Influenza A H3N2A/Wisconsin/67/05
Influenza H1N1 2009A/NY/02/09
Rhinovirus 1A
X2 N. Meningitidis grp A
Influenza B/B/Florida/02/06
Influenza A H1N1A/Brisbane/59/07
Influenza B/B/Malaysia/2506/04
Parainfluenza 1/Type 1
X2 RSV A
RSV B
Influenza A H1N1
2009/A/Canada/6294/09
M. pneumoniae M129
Influenza A H1N1/A/New Caledonia/20/99
Echovirus Type 30
Coxsackie virus Type A9
Validation #16 Negative vial
Influenza A H3N2/A/Brisbane/10/07

Xpert Flu A,B,Flu A 2009 H1N1 RT-PCR Assay

Validation of Gene Xpert using 26 patient specimens were compared to the State Laboratory of Hygiene. ***All were in agreement except one specimen.***	**PCR vs PCR referred** **•15 PCR negative both methods** **• 7 Influenza A positive both methods** **• 3 Influenza B positive both methods** **• *1 Xpert Flu A neg vs WSLH Flu A pos***

LABORATORY-DEVELOPED OR MODIFIED FDA CLEARED / APPROVED TESTS

Good Luck!!



Questions??

http://www.home-building-answers.com/image-files/inspector_pig.jpg