QUALITY CONTROL FOR AST: IQCP?

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WHAT IS QUALITY CONTROL?

- Procedures used to detect errors that occur due to:
  - test system failure
  - adverse environmental conditions
  - variance in operator performance
- AND Monitor the accuracy and precision of the test performance over time
  - CLIA Brochure #4 (2003): Equivalent Quality Control Procedures

MICROBIOLOGY OPTIONS FOR QC

- CLIA regulations
- ~~CLSI guidelines~~
- IQCP

CLIA QC REQUIREMENTS

- QC must detect “immediate” errors
- Basic QC requirement:
  - Two levels of QC materials each day of testing
  - QC material can be:
    - Commercial material
    - Proficiency test specimens (remnant)
    - Patient specimens with known values
    - Split samples with another lab
- Manufacturer’s recommendations must be followed!
  - i.e. your QC procedures cannot be less stringent than those specified by the manufacturer of the test system

NEW INDIVIDUALIZED QUALITY CONTROL PLAN (IQCP)

- Based on CLSI EP-23 "Laboratory Quality Control Based on Risk Management" concepts (but is not EP-23)

EQC	IQCP
Use if manufacturer QC less rigid than regulation	Use if manufacturer QC less rigid than regulation
Transitional	Updated Solution (2016)
Standardized	Customizable
Rigid	Flexible
Analytic	Pre → Post Analytic
Requires internal QC	Does not require internal QC
Decreases external QC	May/may not decrease QC

- Replaces current EQC language in CLIA regulations as of January 1, 2016
  - Like EQC, IQCP is not mandatory
  - Alternative: keep doing 2 levels of daily QC

IQCP (CONTINUED)

- What is IQCP? "Right QC"
  - Risk assessment
  - Quality control plan
  - Quality assessment review

Risk assessment encompasses the entire testing process (preanalytic, analytic, postanalytic) and at minimum, evaluate the following:

- Specimen (collection, labeling, storage, transport, acceptability, etc)
- Environment (temperature, airflow, light, humidity, vibration, utilities)
- Reagent (shipping/receiving, storage conditions, expiration date etc)
- Test system (calibration, mechanical failures, system controls, etc)
- Testing personnel (training, competency, staffing, etc)

http://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/SurveyCertificationGenInfo/Downloads/Survey-and-Cert-Letter-13-54.pdf
(www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Individualized_Quality_Control_Plan_ IQCP.html),

GREAT… MORE PAPERWORK

- True.
- But – this might be an opportunity to identify where errors ARE occurring, and how to mitigate them.

RECENT UCLA AST ERRORS

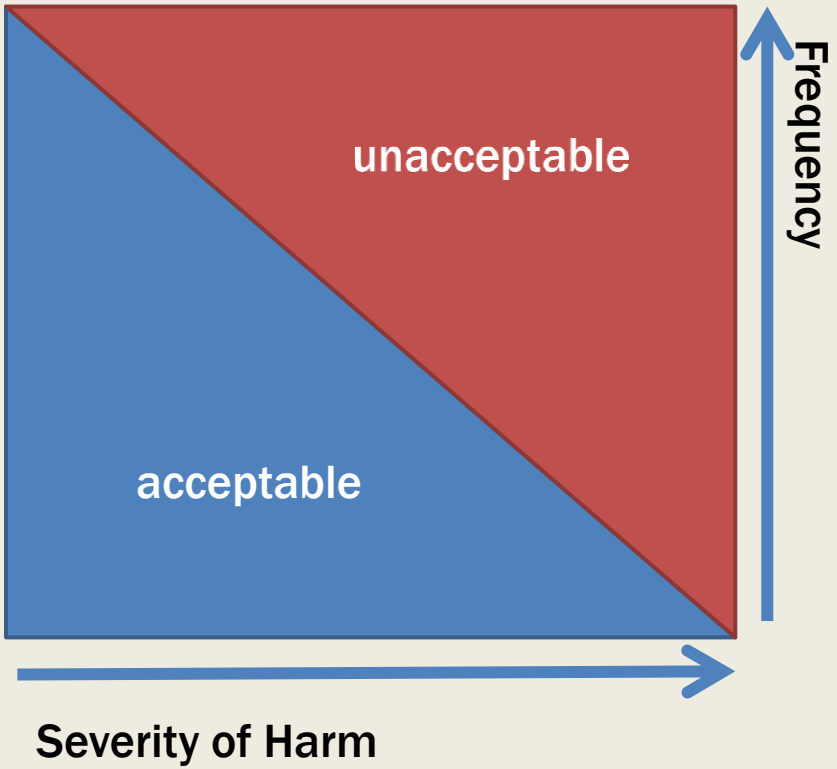
Error	Cause
Pseudomonas aeruginosa reported "S" to ertapenem	Entered with wrong AST panel in computer (Enterobacteriaceae)
MRSA reported as "S" to oxacillin	Computer glitch – editing rules only occur for "*S. aureus*" organism but not "MRSA"
CRE reported as "S-DD" to cefepime off preliminary blood culture AST, repeat testing is "R"	Mixed with *Citrobacter* but missed on initial assessment
S. agalactiae reported as "R" to penicillin	Culture number transposed in error with one growing *Staphylococcus*

QC errors in past year: 0

PART 1: RISK ASSESSMENT

- Laboratory must identify sources of potential failures / errors and evaluate the frequency / impact of these
  - Include in-house data must be used to support number and frequency of QC
    - Verification data, historical QC data, QC information (corrective actions), PT data, competency records for personnel, etc.
  - Can also include published data, package inserts

RISK ASSESSMENT & RISK LEVEL



RISK ASSESSMENT & RISK LEVEL

Severity of Harm →

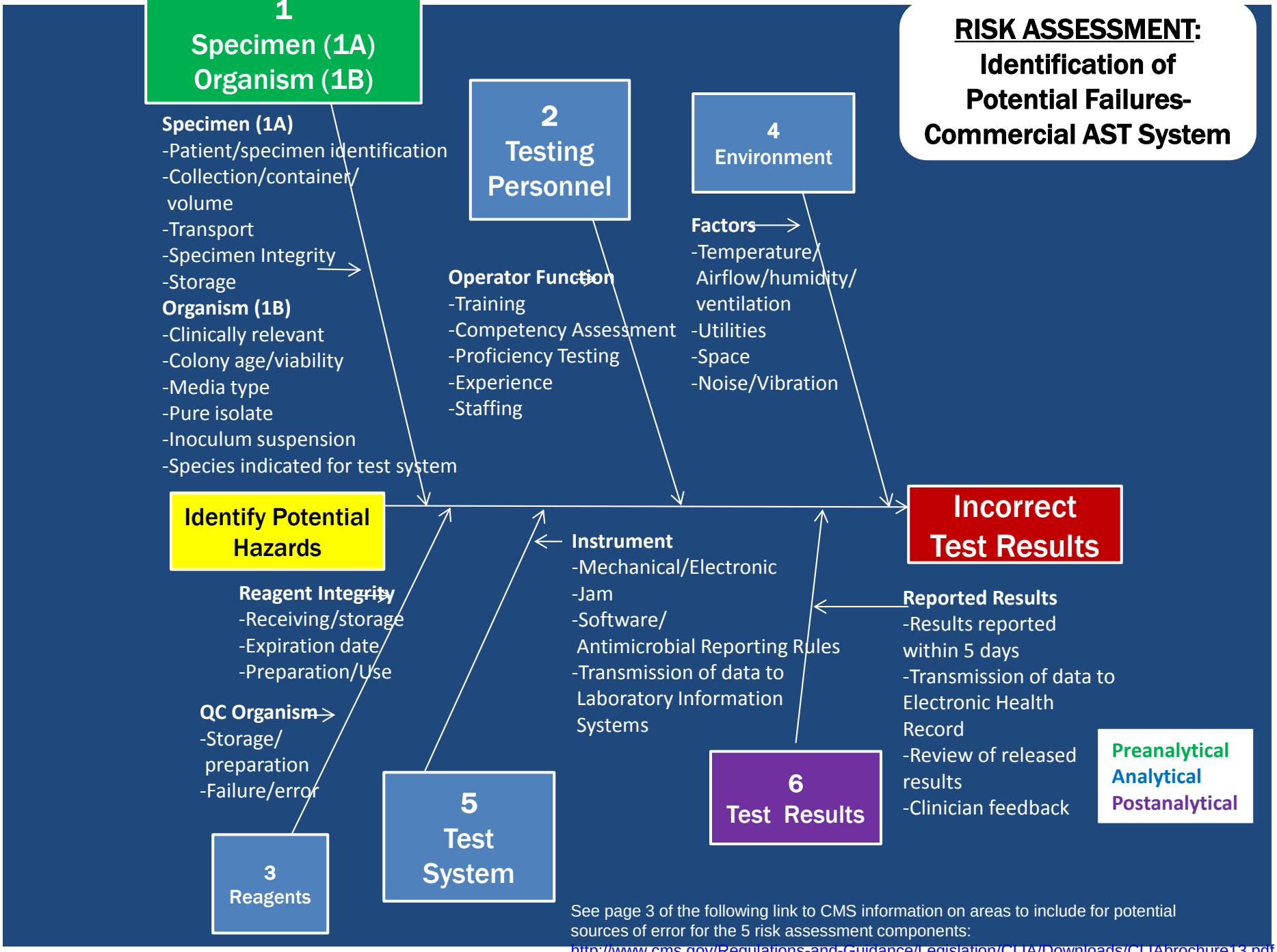
Frequency ↑

	Negligible	Minor	Serious	Critical
Frequent	Not acceptable	Not acceptable	Not acceptable	Not acceptable
Probable	Acceptable	Not acceptable	Not acceptable	Not acceptable
Occasional	Acceptable	Acceptable	Acceptable	Not acceptable
Unlikely	Acceptable	Acceptable	Acceptable	Acceptable

Risk Factor (Possible Sources of Error)	Frequency of occurrence	Severity of harm to patient	Risk Level
Analytical			
Testing Personnel:			
Training	probable	serious	Not Acceptable
Competency	probable	serious	Not Acceptable
Experience	probable	serious	Not Acceptable
Proficiency	unlikely	negligible	Acceptable
Staffing	occasional	minor	Acceptable
Reagents:			
Shipping/receiving/storage	occasional	minor	Acceptable
Expiration dates	unlikely	minor	Acceptable
Preparation/use	probable	minor	Not Acceptable
QC strain storage/prep	occasional	negligible	Acceptable
Environment:			
Temperature/airflow/humidity/ ventilation	unlikely	negligible	Acceptable
Utilities	occasional	minor	Acceptable
Space	unlikely	negligible	Acceptable
Noise/vibration	unlikely	negligible	Acceptable
Test System:			
Mechanical/electronic stability of instrument/equipment/jam	occasional	negligible	Acceptable
Software/antimicrobial reporting rules	frequent	serious	Not Acceptable
Transmission of results to LIS	unlikely	serious	Acceptable
Postanalytical			
Test Results:			
Results reported within 5 days	probable	serious	Not Acceptable
Transmission of results to Electronic Health Record	occasional	serious	Acceptable
Review reported results	frequent	serious	Not Acceptable
Clinician feedback	probable	serious	Not Acceptable

Risk assessment & risk level

http://clsi.org/wp-content/uploads/sites/14/2013/07/CLSI_IQCP_MicroInfo.pdf



See page 3 of the following link to CMS information on areas to include for potential sources of error for the 5 risk assessment components:
http://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/CLIAbrochure13.pdf

EXAMPLE → CRE MIXED WITH CITROBACTER

Risk factor	Possible Error	How to mitigate
Pure isolate	• Mixed inoculum • Contaminated panel	• Regular review on streaking of primary plates • Inoculate purity plate • review of AST profiles as released by technologist • training/competency in reviewing results • Training/competency in risks of testing young colonies • Training/competency in potential sources of contamination during testing • Training/competency in impact of delayed results due to retest

Add reference to your SOP, as applicable

EXAMPLE → OXACILLIN-S MRSA REPORTED

Risk factor	Possible Error	How to mitigate
Review of reported results	• Inappropriate drugs reported • Erroneous results reported • MICs interpreted incorrectly • Report comments missing or inappropriate for culture	• Supervisor maintains summary of incorrect results released and meets with director to review • Training/competency regarding reviewing results prior to reporting • Use “expert” rules on AST system to catch error • Use lab developed “alert” in LIS

PART 2: QUALITY CONTROL PLAN

- QCP must include:
  - Number, type and frequency of QC testing
  - Supported by data in your risk assessment
  - Criteria for acceptability

  - NOTE: QC testing must be no less than that specified in the manufacturer's instructions

HOW OFTEN SHOULD AST QC BE DONE?

- Daily OR
- On days when patient isolates are tested OR
- Weekly (after alternate QC plan implemented)
  - 20 – or 30 – day plan
  - New, alternative 3 x 5 plan

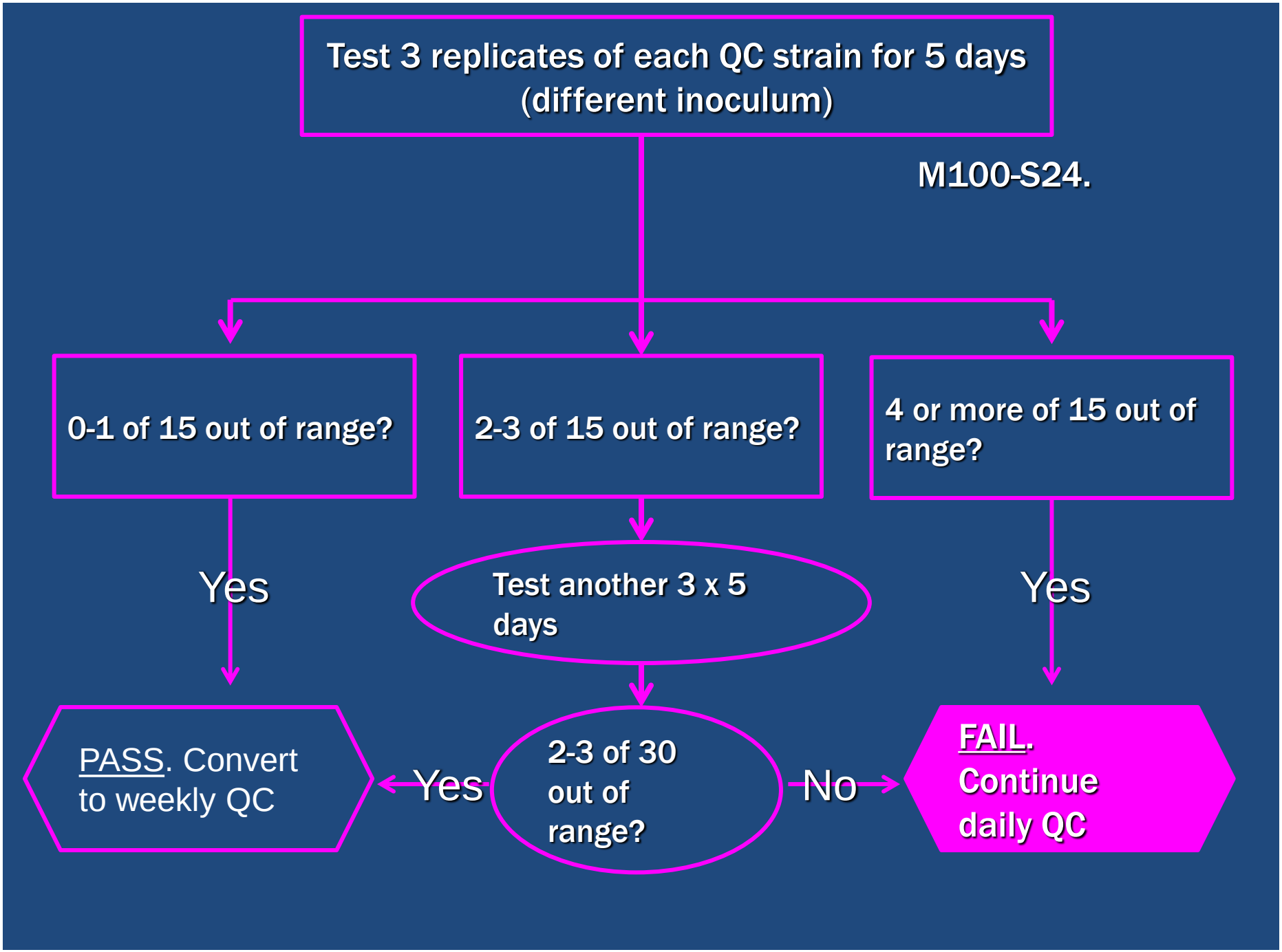
Base this on your risk assessment!

20- 30- DAY PLAN

- Perform testing for 20 or 30 consecutive test days, and document results
- Convert to weekly QC if:
  - No more than 1 out of 20 OR
  - No more than 3 out of 30 MICs for each antimicrobial agent/organism combination are outside acceptable MIC limits
- THEN:
  - Perform weekly QC testing AND
  - Whenever any reagent component of the test is changed (new lot / new shipment)

3 X 5 PLAN

- Perform 3 tests / day for 5 days
  - 3 separate inocula for each replicate
  - If results unacceptable, test another 5 days
- Advantages:
  - Possible to identify issues sooner
  - Takes less time
  - Takes fewer resources
  - Statistically comparable to 20-30 day plan


Test 3 replicates of each QC strain for 5 days (different inoculum)
M100-S24.
0-1 of 15 out of range?
2-3 of 15 out of range?
4 or more of 15 out of range?
Yes
Test another 3 x 5 days
Yes
PASS. Convert to weekly QC
Yes
2-3 of 30 out of range?
No
FAIL. Continue daily QC

WHICH QC STRAIN DO I TEST?

Table 2A. Zone Diameter and Minimal Inhibitory Concentration (MIC) Interpretive Standards for *Enterobacteriaceae*

Testing Conditions

Medium: Disk diffusion: Mueller-Hinton agar (MHA)
Broth dilution: cation-adjusted Mueller-Hinton broth (CAMHB)
Agar dilution: MHA

Inoculum: Growth method or direct colony suspension, equivalent to a 0.5 McFarland standard

Incubation: 35 ± 2°C; ambient air;
Disk diffusion: 16 to 18 hours
Dilution methods: 16 to 20 hours

Routine QC Recommendations (See Tables 4A and 5A for acceptable QC ranges.)

Escherichia coli ATCC®* 25922
***Pseudomonas aeruginosa* ATCC® 27853 (for carbapenems)**
Escherichia coli ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations)

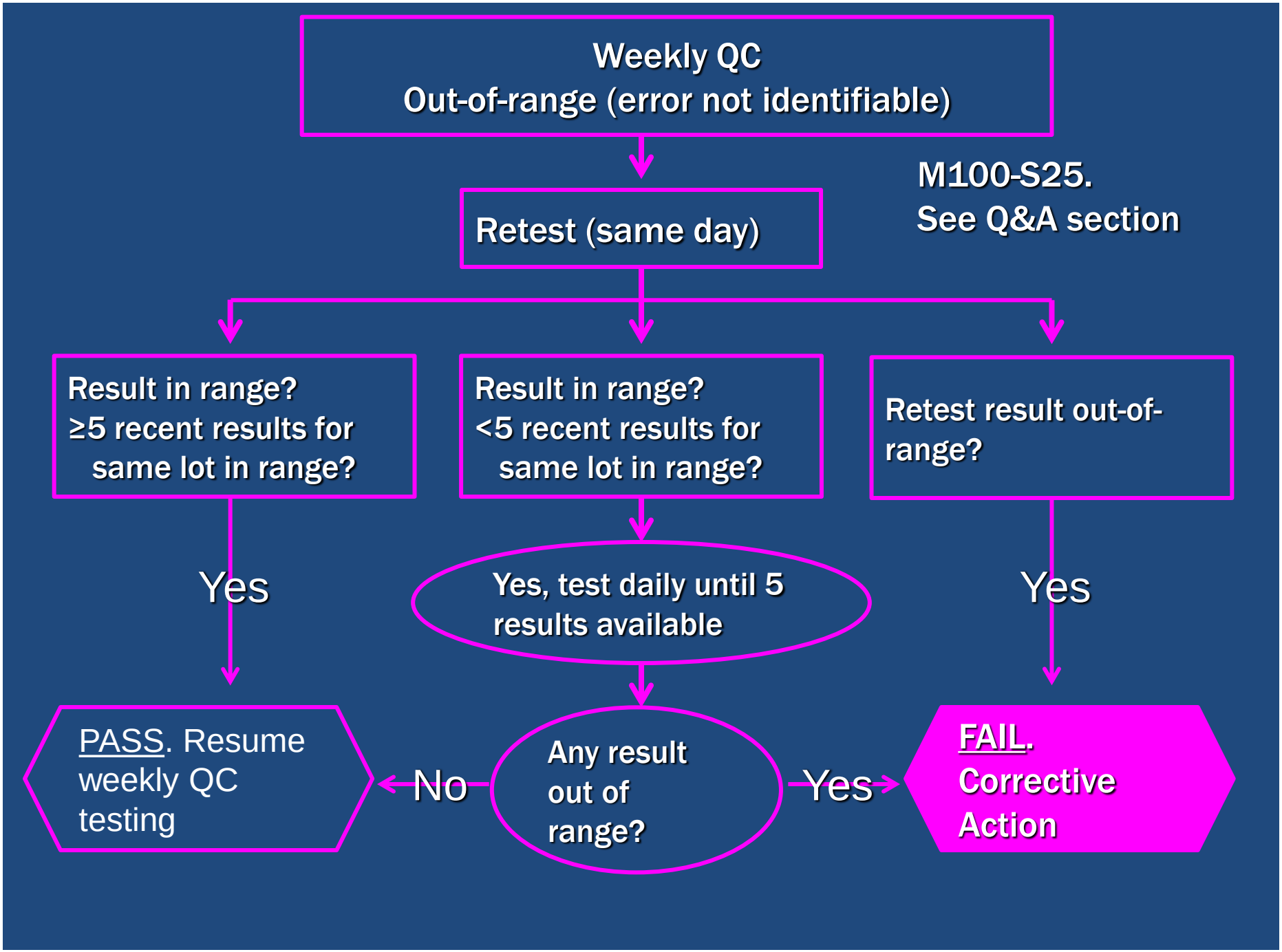
* ATCC is a registered trademark of the American Type Culture Collection.

Refer to Table**s 3A, 3B, and 3C** for additional **testing** recommendations, reporting suggestions, and QC.

IF performing CLSI reference testing (MIC or DD).
IF using a diagnostic manufacturer – follow their QC recommendations!

WHAT ARE THOSE "SUPPLEMENTAL" QC STRAINS FOR?

- "Routine" QC Strain
  - Test regularly (daily or weekly)
- "Supplemental" QC strain
  - May have "S" or "R" characteristic specific for one or more "special" AST tests
    - EXAMPLE: ATCC BAA-977 has includible clindamycin resistance
  - Use to assess new test
  - Use for training purposes
  - Use for competency
  - DO NOT need to perform regularly (weekly or daily)


Weekly QC
Out-of-range (error not identifiable)
M100-S25.
See Q&A section
Retest (same day)
Result in range?
≥5 recent results for same lot in range?
Result in range?
<5 recent results for same lot in range?
Retest result out-of-range?
Yes
Yes, test daily until 5 results available
Yes
PASS. Resume weekly QC testing
No
Any result out of range?
Yes
FAIL. Corrective Action

EXAMPLES

E. Coli ATCC 25922 and ampicillin
Acceptable Range: 2-8 µg/ml
Lot: 9661

Scenario 1

Week	Day	Result	Action
1	1	4	
2	1	8	
3	1	8	
4	1	4	
5	1	16	Out of QC, repeat next day
5	2	8	In range. 5 acceptable QC tests

Scenario 2

Week	Day	Result	Action
1	1	4	
2	1	8	
3	1	16	Out of QC, repeat next day
3	2	4	In range: 3 acceptable results (need 2 more)
3	3	8	In range
3	4	8	In range. 5 acceptable QC tests

UH-OH, MORE RESULTS OUT OF QC!

- Probable system error
- Daily QC must be continued until final resolution of problem!
- Ideas on how to fix this:
  - New QC strain
  - New lots of materials (incl. new turbidity standards)
  - If problem appears to be related to manufacturer, contact them!
  - Might need to use another test method
- QC ranges are established to include >=95% of results from routine testing
  - Some errors are random!

WHAT ABOUT MY PATIENT RESULTS?

- Don’t forget to carefully review each patient result
- Approaches will differ, based on degree and direction of QC errors
- Things to consider:
  - Suppress result for antimicrobial out of QC
  - Review individual patient / cumulative data for unusual patterns (should be doing this anyway)
  - Use an alternative method if necessary

SOURCES OF ERROR IDENTIFIABLE BY QC TESTING

- Wrong QC strain used
- Improper storage of QC strain
- Inadequate maintenance of QC strain (same F2 for >1 month)
- Contamination of QC strain
- Nonviable QC strain
- Changes (loss of plasmid) to QC strain

- Improper storage of reagents
- Contamination of reagents
- Damages plates / panels
- Expired reagents
- Not following SOP
- Transcription error
- Equipment problems

What about everything else I identified in my risk assessment??

PART 3: QUALITY ASSESSMENT

- "Post-Implementation Monitoring Process" allows you to identify when a process is in need of review/revision.
- May include the review and monitoring of the following:

- Proficiency testing
- Personnel training
- Personnel competency assessments
- Unexpected errors, investigations, and remediation
- Statistics
  - Positivity rates
  - Standard Deviation
  - Coefficient of Variance
- Failure rates
  - Technical competency?
  - Instrumentation?
- Complain investigation / remediation

EXAMPLE OF COMPETENCIES TO CHECK FOR AST

Competencies	Competencies (cont.)
Appropriately determines which orgs require AST	Maintains and subcultures QC strains appropriately
Uses appropriate inoculum preparation method	Runs daily / weekly QC
Prepares inoculum correctly	Reads and documents QC results appropriately
Tests agents or panel appropriate for organism	Identifies and troubleshoots out of QC results
Inoculates test correctly	Performs problem solving in AST
Incubates correctly	Maintains appropriate inventory of supplies
Confirms purity checks before recording results	Handles all testing materials appropriately
Reads, records, interprets correctly	Performs/documents AST instrument maintenance
Verifies profile and organism prior to reporting	Locates current CLSI standards
Takes appropriate action to confirm unusual results	
Reports appropriate agents / comments	
Uses computer appropriately for reporting	
Notifies supervisor, IC, physician of atypical results	
Consults with physician on special AST requests	

These can be measured by:

1. Direct observation (Best)
2. Monitoring of recording/reporting of test results
3. Review of worksheets, QC, PT, PM records
4. Assessment of problem solving skills

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REVIEW OF UNUSUAL RESULTS

- Every AST profile for every organism should be reviewed before reporting!!
- Why?
  - Testing routine QC strains doesn't ensure every result on a patient's isolate is accurate
- Patient results may be erroneous due to:
  - mixed culture, misidentification
  - individual drug/bug problem
  - other technical errors

EXAMPLE: SUPERVISOR REVIEW OF DAILY RESULTS

- *S. agalactiae* isolated from blood and wound cultures from an 82 year old woman with diabetes and right ankle pain / swelling

Penicillin	0.06	S
Cefotaxime	0.12	S
Clindamycin	>32	R
Erythromycin	>32	R
Vancomycin	4	NS

Review of Patient Results:

- Do ID and AST results correlate?
- Were appropriate drugs reported?
- Are results from similar drugs (class) OK?
- Were appropriate comments added?

EXAMPLE

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Review of Patient Results:

- Do ID and AST results correlate? ✗
- Were appropriate drugs reported? ✔
- Are results from similar drugs (class) OK? ✔
- Were appropriate comments added? ✗

APPENDIX A M100 S24

Appendix A. (Continued)

Organism or Organism Group	Resistance Phenotype Detected[a]	Occurrence and Significance of Resistance and Actions to Take Following Confirmation of Results[a]		
		Category I	Category II	Category III
		Not reported or only rarely reported to date	Uncommon in most institutions	May be common, but is generally considered of epidemiological concern
Streptococcus pneumoniae	**Ceftaroline – R** Linezolid – NS Vancomycin – NS	x		
	Fluoroquinolone – I or R Imipenem or meropenem – I or R Quinupristin-dalfopristin – I or R Rifampin – I or R		x	
	Using nonmeningitis breakpoints: Amoxicillin or penicillin – R Extended-spectrum cephalosporin[c] – R			x
Streptococcus, β-hemolytic group[g]	Ampicillin or penicillin – NS **Ceftaroline – NS** Daptomycin – NS Ertapenem or meropenem – NS Extended-spectrum cephalosporin[c] – NS Linezolid – NS Vancomycin – NS	x		
	Quinupristin-dalfopristin – I or R		x	
Streptococcus, viridans group	Daptomycin – NS Ertapenem or meropenem – NS Linezolid – NS Quinupristin-dalfopristin – I or R Vancomycin – NS	x		

STEPS THAT SHOULD HAVE BEEN TAKEN TO CONFIRM UNUSUAL ID/AST:

- Check for transcription errors, contamination, or defective panel, plate, or card.
- Check previous results for the patient to determine if the isolate was encountered and confirmed
- Repeat organism ID and AST with initial method to ensure they reproduce.
- Confirm ID with second method performed in-house or at a referral laboratory.
- Confirm AST results with second method (eg, in-house or referral laboratory). The second method might be:
  - CLSI reference method (eg, BMD, or DD) or
  - An FDA-cleared commercial test.
- Notify Supervisor / Infection Control of unusual result, if confirmed

DON'T WORRY - THERE IS A GREAT RESOURCE:

- Individualized Quality Control Plan (IQCP) PowerPoint® Template for use with Commercial MIC Antimicrobial Susceptibility Testing (AST) Systems t

http://clinmicro.asm.org/iqcp