MEDICAL DEVICE RECALLS: A PRACTICAL APPROACH AND CALL FOR HELP

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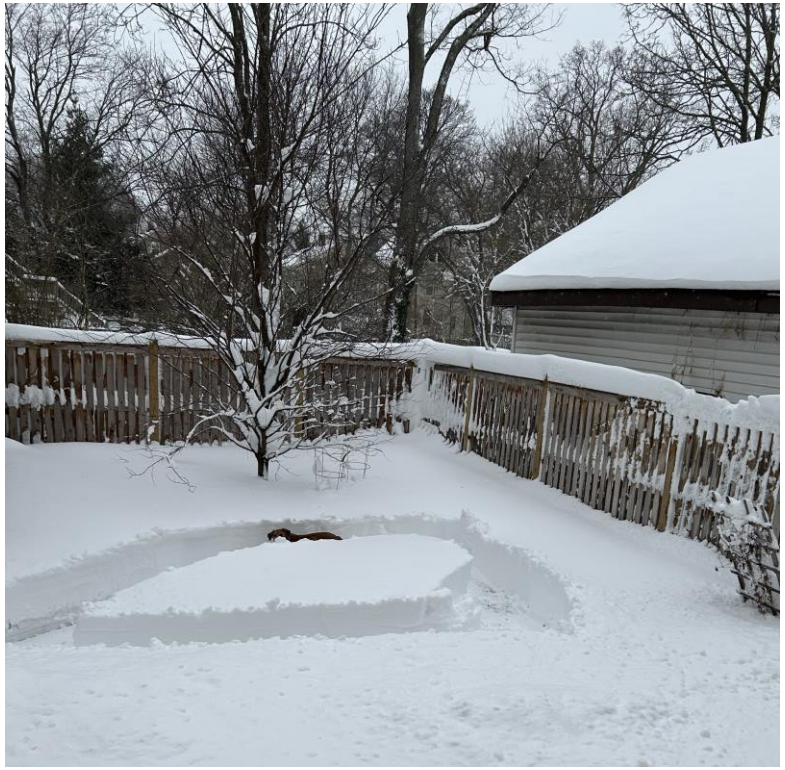
DISCLOSURES

- Yale University: Employment
- VA CT Healthcare: Employment
- Hologic: Research Support
- BD: Honoraria / Advisory Board

- *All of the relevant financial relationships listed for this individual have been mitigated.*

WINTER HAS BEEN ROUGH



GOALS AND OUTLINE

- Present key questions for how to approach manufacturer device recalls within the context of laboratory quality management
- Present 3 examples of recalls in the context of that framework: HBV FP, GBS FN, HCV Ab WTF
- Discuss vendor actions that could ease laboratory burden when dealing with device recalls

QUESTIONS (SHOW OF HANDS)

- What roles do we have in the audience today?
- Who has received a product recall notification?
- Do you have a form or SOP for addressing recalled IVD assays?
- Have you spent more than 10 hours dealing with a single recall?
- How have you communicated recalls? Provider letter? Patient letter? Provider phone call? Patient phone call?
- Do you have an adverse patient event that you ascribe to a recalled IVD assay?

RECALLS FROM FDA PERSPECTIVE

- Things to keep in mind:
  - FDA is focused on manufacturers and manufacturer compliance with regulations
  - Lab tests = medical devices
  - Recall framework makes a little more sense for non-assay medical devices
- How is a recall initiated?
  - Voluntary recall initiated by manufacture
  - Mandatory recall initiated by FDA
- Recalls can be either ***removals*** or ***corrections***

- Why initiate a medical device recall?
  - ***Device is defective and/or device is a risk to health***
  - For lab tests, common examples include:
    - Labeling or design defect that impacts device performance or safety (e.g. software, power supplies, other design feature / failure)
    - Identification of factors where device performance specifications are not met
      - Assay accuracy issues exceeding those outlined in IFU
      - Identifiable and/or reproducible issues causing deviations from expected performance

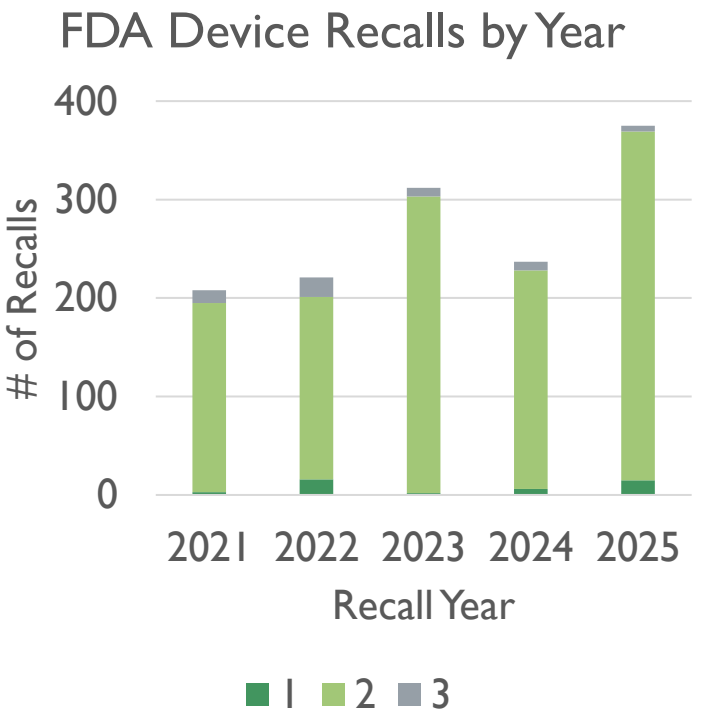
FDA ASSESSMENT OF HEALTH HAZARDS

- Whether any disease or injuries **have already occurred** from the use of the product.
- Whether any existing conditions **could contribute** to a clinical situation that could expose humans or animals **to a health hazard**.
- Assessment of hazard to **various segments of the population**, e.g., children, surgical patients, pets, livestock, etc.
- Assessment of the degree of **seriousness of the health hazard** to which the populations at risk would be exposed.
- Assessment of the **likelihood of occurrence** of the hazard.
- Assessment of the **consequences** (immediate or long-range) of occurrence of the hazard.

Potential health hazards are considered together to determine recall class

HOW ARE RECALLS CLASSIFIED?

Recall Class	Explanation
Class 1	**Reasonable probability** that the use of or exposure to **will cause serious adverse health consequences or death**.
Class 2	Use of, or exposure to **may cause temporary or medically reversible adverse health consequences** or where the **probability of serious adverse health consequences is remote**.
Class 3	Use of, or exposure to is **not likely to cause adverse health consequences**.



N.B. In 2025 2 companies were responsible for 110 Recalls for lack of PMA (n = 86) and lack of manufacturing standards (n = 24)

WHAT INFORMATION DO WE EXPECT TO RECEIVE

- Brand name and common name of the device and intended use.
- FDA marketing status, i.e., 510(k), PMA, pre-amendment status and device listing number.
- Model/catalog number, lot/serial number
- Date of manufacture or distribution; expiration date or expected life.
- ***Description of event(s) and the corrective and removal actions that have been and are expected to be taken.***
- Any illness or injuries that have occurred with the use of the device.

WHERE DO MEDICAL DEVICE RECALLS "LIVE" FOR QM PURPOSES?

G. **Nonconforming event management**

1. Establish an open communication for reporting nonconforming events to support the clinical virology laboratory's quality system. Examples of nonconforming events include provider complaints, failed QC or PT results, errors in patient results or reports, malfunctioning instruments, reagents or consumables, laboratory personnel concerns, issues identified by internal or external audits, manufacturer recalls, etc.
2. Establish a system for accurately tracking laboratory errors and their occurrence. Analyze errors and take corrective action.
3. Implement review processes for detection of laboratory errors. These may include comparisons of requisition forms to specimen labels, comparisons of final results to instrument testing logs, and review of QC failures and repeat test runs.
4. Investigate errors reported directly by health care providers or via online systems.
5. Document investigations and resolutions of nonconforming events using defined incident reports. Reports should be reviewed by the laboratory director or designee.
6. Determine the medical significance and impact of errors on patient care and management.

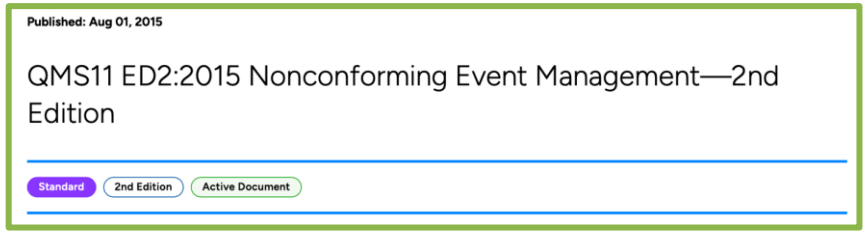
Places manufacturer recalls within larger nonconforming event framework

Clinical Microbiology Procedures Handbook

Yale School of Medicine

MEDICAL DEVICE RECALLS ARE NON-CONFORMING EVENTS (NCE)

- APHL
  - A deviation from the standard operating procedure or conditions required to accurately complete testing and report an accurate test result.
- CLSI
  - An occurrence that does not conform to the laboratory's policies, processes, and/or procedures, or
  - Does not conform with applicable regulatory or accreditation requirements, or
  - Has the potential to affect (or has affected) patient, donor, or employee safety.



WHAT DOES CAP SAY ABOUT THIS?

GEN.20208 Identification of Non-conforming Events **Phase II**

The QMS includes a process to identify and record non-conforming events.

GEN.20340 Notifications From Vendors **Phase II**

GEN

The laboratory manages notifications from vendors of defects or issues with reagents, supplies, instruments, equipment, or software that may affect patient care/client services.

NOTE: Notifications may take the form of product recalls, market withdrawals, or software patches and upgrades. The laboratory must take timely action on those that have the potential to affect testing results or laboratory services. The laboratory must have appropriate processes to address notifications that may be initially received by different departments (eg, purchasing) to avoid delays associated with handoff communications.

Clinic

Evidence of Compliance:

- ✓ Records of manufacturer's recalls received **AND**
- ✓ Records of follow-up

- Must take timely action that have *potential to affect results or services*
- Must have process to *address notifications initially received by different departments*

GENERAL NCE PRACTICE V. DEVICE RECALL

Laboratory Error or Quality Issue

- NCE occurred within laboratory
- Initiated by laboratory by self-identification or upon report by patient / provider
- Laboratory (potentially) deviated from expected / standard practice in some way
- Within laboratory / institution investigation, potentially including root cause analysis, will be performed

Device Recall

- NCE occurred outside laboratory
- Initiated by manufacturer
- Laboratory itself had no deviation from standard practice
- Root cause analysis not indicated unless adverse event and institutional policy dictate

Shared Practices

- Local determination of NCE scope
- Notification of affected laboratories / providers / patients
- Assessment of potential patient harm
- Responsive action taken for NCE

GENERAL NCE PRACTICE V. DEVICE RECALL

Laboratory Initiated NCE Investigation

Detailed Investigation of Laboratory Practices

+

Assessment of Potential Patient Impact

Recall Related Investigation

Detailed Investigation of Laboratory Practices

+

Assessment of Potential Patient Impact

RISK MATRIX AND INVESTIGATIONS

	High severity	Moderate severity	Low severity
High probability	Corrective action to eliminate root cause	Corrective action to eliminate root cause	Correction of immediate problem
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If the Risk Is:	Speed of Investigation	Persons Usually Involved
High	• Fast process • May need more complex actions • In-depth investigation • Time sensitive	May expand to other departments or organizations
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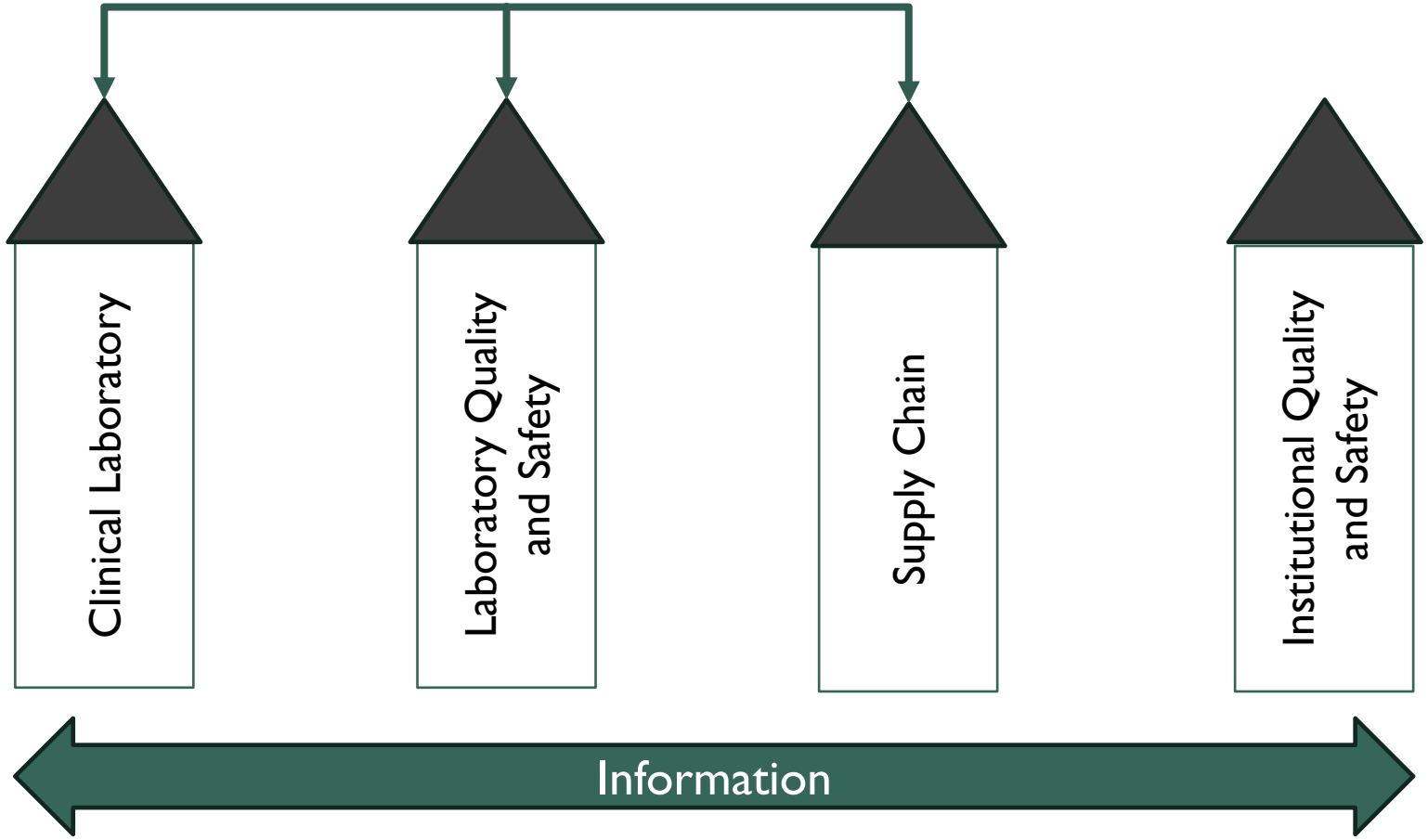
Device recalls often call for immediate cessation of testing

COMMUNICATION IS KEY

Multiple Potential Points of Entry



*These are silos

HOW ARE DEVICE RECALLS COMMUNICATED

EXTERNAL EMAIL

DO NOT click links or open attachments unless you trust the sender AND know the content is safe.

====DO NOT REPLY TO THIS E-MAIL====

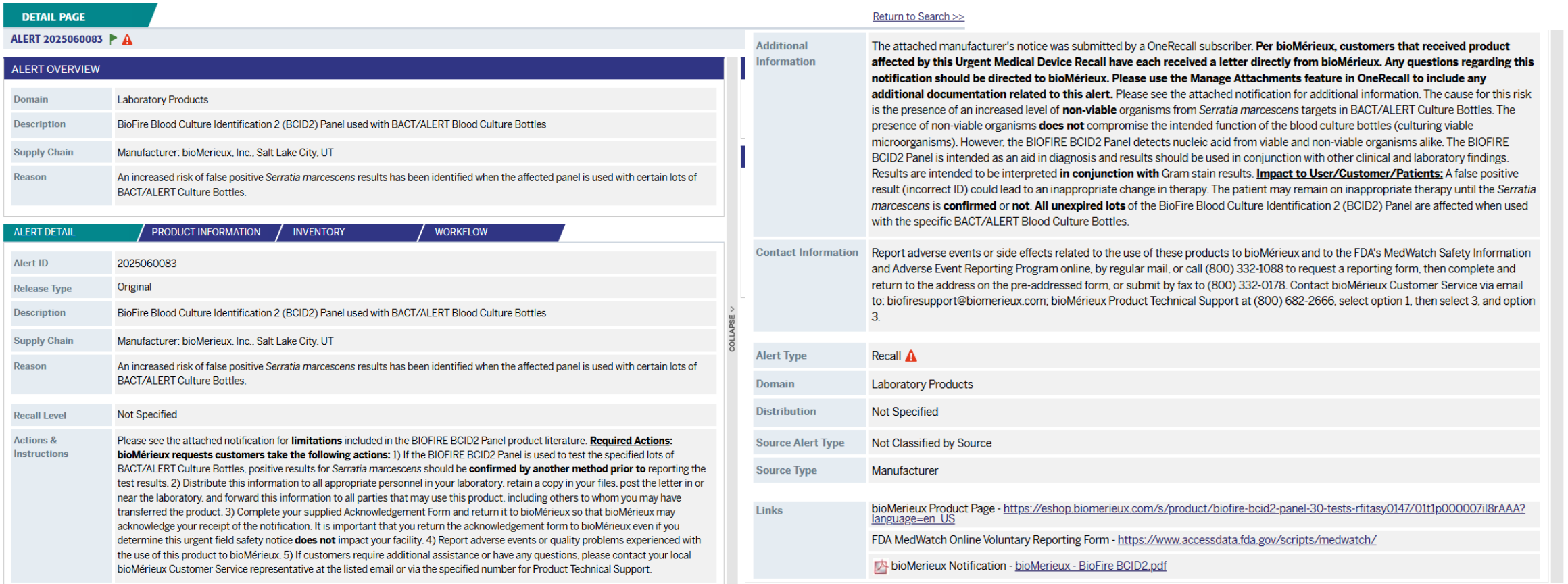
For assistance with this alert, contact your OneRecall manager.

If you have questions, suggestions or comments about OneRecall, contact Customer Support at https://urldefense.com/v3/__https://onerecall.inmar.com/?page_id=7__;!!G9aKEII32E6ngQ!Mw0wHwBZg_EqJBeIKIcMFcDCWeSIssarKS0DVaVFtQQxhRGFVjc-odH5kTHbETIW2cgAzHDAkzTNI39BATbb0OcX5C5lpA$

Vendor "Dear Customer" Email

Institutional Quality and Safety Email

STANDARDIZED RECALL INFORMATION



DETAIL PAGE

Return to Search >>

ALERT 2025060083

ALERT OVERVIEW

Domain	Laboratory Products
Description	BioFire Blood Culture Identification 2 (BCID2) Panel used with BACT/ALERT Blood Culture Bottles
Supply Chain	Manufacturer: bioMerieux, Inc., Salt Lake City, UT
Reason	An increased risk of false positive *Serratia marcescens* results has been identified when the affected panel is used with certain lots of BACT/ALERT Culture Bottles.

ALERT DETAIL | PRODUCT INFORMATION | INVENTORY | WORKFLOW

Alert ID	2025060083
Release Type	Original
Description	BioFire Blood Culture Identification 2 (BCID2) Panel used with BACT/ALERT Blood Culture Bottles
Supply Chain	Manufacturer: bioMerieux, Inc., Salt Lake City, UT
Reason	An increased risk of false positive *Serratia marcescens* results has been identified when the affected panel is used with certain lots of BACT/ALERT Culture Bottles.
Recall Level	Not Specified
Actions & Instructions	Please see the attached notification for **limitations** included in the BIOFIRE BCID2 Panel product literature. **Required Actions: bioMérieux requests customers take the following actions:** 1) If the BIOFIRE BCID2 Panel is used to test the specified lots of BACT/ALERT Culture Bottles, positive results for *Serratia marcescens* should be **confirmed by another method prior to** reporting the test results. 2) Distribute this information to all appropriate personnel in your laboratory, retain a copy in your files, post the letter in or near the laboratory, and forward this information to all parties that may use this product, including others to whom you may have transferred the product. 3) Complete your supplied Acknowledgement Form and return it to bioMérieux so that bioMérieux may acknowledge your receipt of the notification. It is important that you return the acknowledgement form to bioMérieux even if you determine this urgent field safety notice **does not** impact your facility. 4) Report adverse events or quality problems experienced with the use of this product to bioMérieux. 5) If customers require additional assistance or have any questions, please contact your local bioMérieux Customer Service representative at the listed email or via the specified number for Product Technical Support.

COLLAPSE

Additional Information	The attached manufacturer's notice was submitted by a OneRecall subscriber. **Per bioMérieux, customers that received product affected by this Urgent Medical Device Recall have each received a letter directly from bioMérieux. Any questions regarding this notification should be directed to bioMérieux. Please use the Manage Attachments feature in OneRecall to include any additional documentation related to this alert.** Please see the attached notification for additional information. The cause for this risk is the presence of an increased level of **non-viable** organisms from *Serratia marcescens* targets in BACT/ALERT Culture Bottles. The presence of non-viable organisms **does not** compromise the intended function of the blood culture bottles (culturing viable microorganisms). However, the BIOFIRE BCID2 Panel detects nucleic acid from viable and non-viable organisms alike. The BIOFIRE BCID2 Panel is intended as an aid in diagnosis and results should be used in conjunction with other clinical and laboratory findings. Results are intended to be interpreted **in conjunction with** Gram stain results. **Impact to User/Customer/Patients:** A false positive result (incorrect ID) could lead to an inappropriate change in therapy. The patient may remain on inappropriate therapy until the *Serratia marcescens* is **confirmed** or **not**. **All unexpired lots** of the BioFire Blood Culture Identification 2 (BCID2) Panel are affected when used with the specific BACT/ALERT Blood Culture Bottles.
Contact Information	Report adverse events or side effects related to the use of these products to bioMérieux and to the FDA's MedWatch Safety Information and Adverse Event Reporting Program online, by regular mail, or call (800) 332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to (800) 332-0178. Contact bioMérieux Customer Service via email to: biofiresupport@biomerieux.com; bioMérieux Product Technical Support at (800) 682-2666, select option 1, then select 3, and option 3.
Alert Type	Recall
Domain	Laboratory Products
Distribution	Not Specified
Source Alert Type	Not Classified by Source
Source Type	Manufacturer
Links	bioMerieux Product Page - https://eshop.biomerieux.com/s/product/biofire-bcid2-panel-30-tests-rfitasy0147/01t1p000007il8rAAA?language=en_US FDA MedWatch Online Voluntary Reporting Form - https://www.accessdata.fda.gov/scripts/medwatch/ bioMerieux Notification - bioMerieux - BioFire BCID2.pdf

GENERAL FACTORS THAT COULD AFFECT YOUR INVESTIGATION AND RESPONSE

Laboratory Factors

- How much reference / outreach testing do you do?
  - Do you have access to medical records for chart review?
  - Are most of your providers under your corporate umbrella?
- Where does the burden of investigation and notification fall?
  - Laboratory quality and safety? Outreach? Lab director and manager?

Institutional Factors

- What are your institutional policies regarding investigation and notification?
- What are your institutional expectations regarding notification and communication?
- Are there local experts who:
  - Will be consulted either directly or indirectly?
  - Care for many / most affected patients?

DISEASE SPECIFIC FACTORS TO CONSIDER

Disease + Test Specific Factors

- Is the condition acute and self-limited? Chronic with recurrent monitoring?
- Is testing for asymptomatic surveillance / screening?
- Are there specific interventions undertaken as a direct result of testing?
- Is disease diagnosis based upon a single result? A multi-step algorithm?
- Are there mitigation strategies for erroneous / absent results?

Possible Actions from Tests

- Withholding / Adding / Changing Therapy
- Procedure cancellation / Unnecessary invasive procedure
- Additional laboratory draws
- Inappropriate isolation precautions
- Escalation of setting of care
- Work / School / Day Care implications

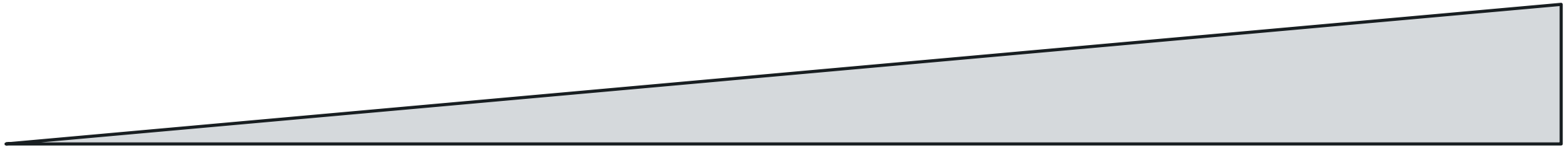
POTENTIAL ACTIONS

- Confirm your testing was affected and determine preliminary scope of problem
- Assess severity of risk of recall
- Confer with laboratory leadership including quality and safety to determine approach
- Confer with institutional quality and safety if appropriate, esp. if potential significant impact
- Identify affected samples → patients → providers by LIS / EMR / Instrument queries
- Do what the recall says: stop testing, re-test, confirm, etc.
- Communication with sending labs (for reference labs)
- Communication with providers
- Chart review to assess for adverse events esp. potentially significant

Almost all response require knowledge of specimens, patients, and providers affected → correlation of instrument and LIS / EMR data

RANGE OF RESPONSES

Less Work for Lab ***More Work for Lab***



100% Generic "Dear Laboratory" / "Dear Provider" Letter

Some case finding with narrowed communication

Detailed retrospective data analysis for case finding

Patient specific chart review with specific communication

Root Cause Analysis or equivalent

MY SETTINGS FOR TESTING

Yale New Haven Health

- Five hospitals over seven campuses totaling 2,700 beds (1,600 at YNHH)
- Most microbiology and virology testing is centralized to New Haven
- Most testing is done for affiliated providers with some outreach testing
- Users of "YNHHS EPIC" also include affiliated university health plan and local FQCHCs

Virology Reference Laboratory @ VACT

- Reference laboratory for 6 New England VAs (VISN1) + a few other VAs
- Distribution of volume varies by assay but roughly 1/3 CT, 1/3 MA, and 1/3 RI + NH + VT + ME
- Laboratory testing and communication is coordinated at VISN-level to some extent
- EMR is location specific - ish

- Generally high expectations for communication within laboratory leadership
- Both at different stages of "high reliability organization" journey
- Affiliated specialty services across most relevant disciplines
- Some support for investigations, but burden mostly on laboratory staff

HBV QUANT DNA FALSE POSITIVES

Dear [redacted] Customer,

This letter contains important information regarding the [redacted] HBV [redacted] Kit, [redacted] utilized with the [redacted] System. Please review this information carefully.

Background
[redacted] has received reports of falsely elevated results when using the [redacted] HBV [redacted] Kit. Data analysis has determined that carryover from a well containing high titer HBV to a neighboring well is a potential contributing factor.

Potential Impact
Carryover events may cause samples that are positioned near positive samples in the assay tray to produce falsely elevated (misquantitation high) HBV results.

[redacted] investigated the situation and conducted additional carry over studies. Carryover values observed in the study into negative samples were under 2000 IU/ml[1]. We plan to update the Carryover and Limitations of the Procedure sections of the associated package insert with the following information:

Carryover:
The carryover rate for [redacted] HBV was determined by analyzing 774 valid replicates of HBV negative samples processed from alternating positions with 770 valid replicates of high concentrated HBV positive samples at 100,000,000 IU/mL, across multiple runs. HBV DNA was detected in 16 of the HBV negative samples, resulting in an overall carryover rate of 2.1% (95% CI: 1.2 to 3.3%).

Limitations of the Procedure:
Unexpected HBV DNA levels due to carry over may occur. If results are inconsistent with patient history and other diagnostics through patient monitoring, a retest of the sample should be considered by the physician or healthcare provider.

While there is potential impact to results for [redacted] HBV, there is no impact or change to the assay reagents. There have been zero (0) reports received to-date of harm associated with this

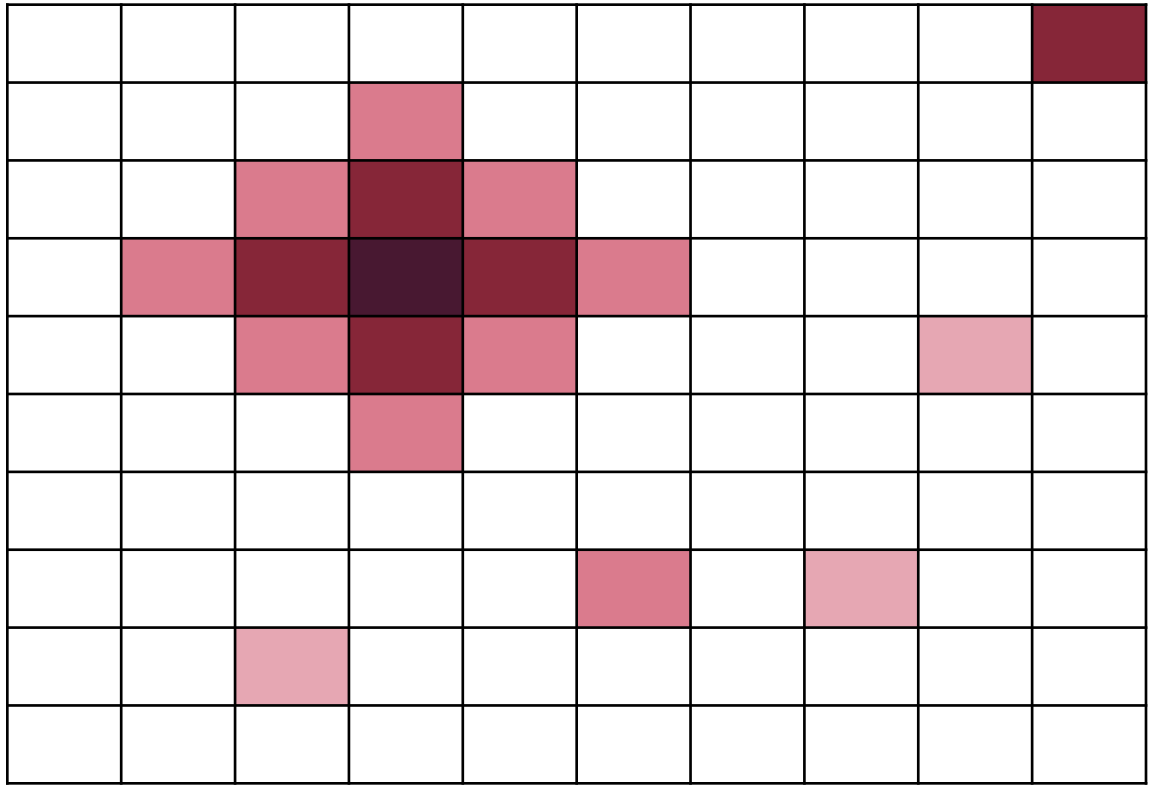
Summary

- Falsely elevated HBV viral load results
- Carry-over from ”near positive samples in the assay tray”
- 2.1% Carry-over for 10^8 IU / mL to negative samples
- Affected samples gave results < 2000 IU / mL (<LLOQ to 1,700)
- Positive control is ~10^4 IU / mL

ASSUMPTIONS ABOUT CARRY-OVER

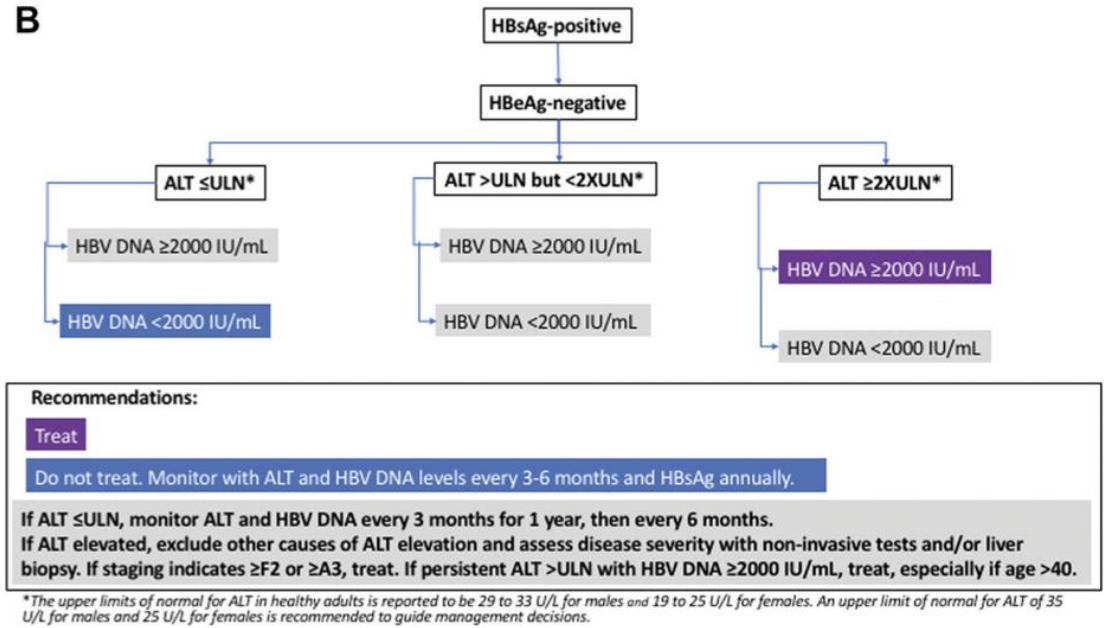
- Negative samples not affected
- Runs with only a single positive not affected
- Highest titer samples on run not affected
- There should be a substantial dilution from positive sample to false positive sample

- ***If positive control(s) cause carry-over to patient samples, this could be an issue***
- ***Inner workings of instrument / pipetting may not be obvious***



POTENTIAL CLINICAL IMPACT OF FALSE POSITIVE HBV QUANT

- What is the test used for?
  - Disease monitoring in patients with chronic HBV infection
  - Not sole basis for diagnosis or monitoring; often recurrent testing
  - Might be used in assessment of seroreactive patients about to undergo immunosuppression
- How might results be used?
  - Modification of anti-viral regimens
  - Administration of prophylaxis prior to immunosuppression
  - Request for anti-viral resistance testing
- Viral Load > 2,000 IU / mL is important inflection point



RISK MATRIX AND INVESTIGATIONS

	High severity	Moderate severity	Low severity
High probability	Corrective action to eliminate root cause	Corrective action to eliminate root cause	Correction of immediate problem
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If the Risk Is:	Speed of Investigation	Persons Usually Involved
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Low	• Slower process • May need only minimal actions • Simpler investigation • Data collected and analyzed later	Laboratory

Moderate probability of moderate severity harm

ACTIONS

- Temporarily stopped testing; Batched runs 2x week
- Review HBV viral load data to determine scope of problem
  - HBV Viral Load by date / run
  - HBV serology results if available
- Laboratory Records Review
  - All positive results generated by instrument included
  - 65 positive patients → Most excluded
    - Single positive in batch
    - All results in batch comparable / >> 2,000 IU / mL
- Communicated with local hepatology clinic
- Communicated with laboratories using as reference laboratory
- Assessed no patient harm

GBS FALSE NEGATIVE

[redacted]

URGENT: MEDICAL DEVICE RECALL NOTIFICATION

SIGNATURES ON FILE

[redacted]

Distribution: United States and Canada

Purpose

This is to inform you of a recall of the [redacted] GBS assay that is being initiated voluntarily by [redacted]

Due to increasing variability in global supply chain and raw materials associated with this product, there is a potential that the product does not meet the performance claims as specified in the Package Insert. Specifically, samples that have analyte concentrations that are at or near the Limit of Detection (LoD) may produce false negative results. [redacted] is not aware of any cases of incorrect results reported due to this issue. Given the risk associated with false negative GBS results, [redacted] is recalling the lots listed in Table 1 below and is discontinuing the further sale of the [redacted] GBS Assay, catalog number [redacted] for the foreseeable future.

Table 1: List of Affected Lots of [redacted] GBS Reagent

Product	Catalog Number	Lot numbers	Distribution Dates
[redacted] GBS Assay Cartridges 96 Tests	[redacted]	274954 284599 296991 300796 309230 309353	Aug. 26, 2020 to Feb. 10, 2022

Summary

- Potentially falsely-negative GBS PCR results
- Manufacturing issue caused expected assay performance (LOD) to deviate from IFU
- Theoretical risk; no reported adverse events
- Risk was assessed analytically WITHOUT broth enrichment

GBS PCR USED FOR ANTENATAL GBS SCREENING

Test Use

- Antenatal screening for GBS to prevent early onset sepsis in neonates (severe adverse event)
- Obtained at weeks 36 to 37 during pregnancy

Table 1. Indications for Intrapartum Antibiotic Prophylaxis to Prevent Neonatal Group B Streptococcal Early-Onset Disease

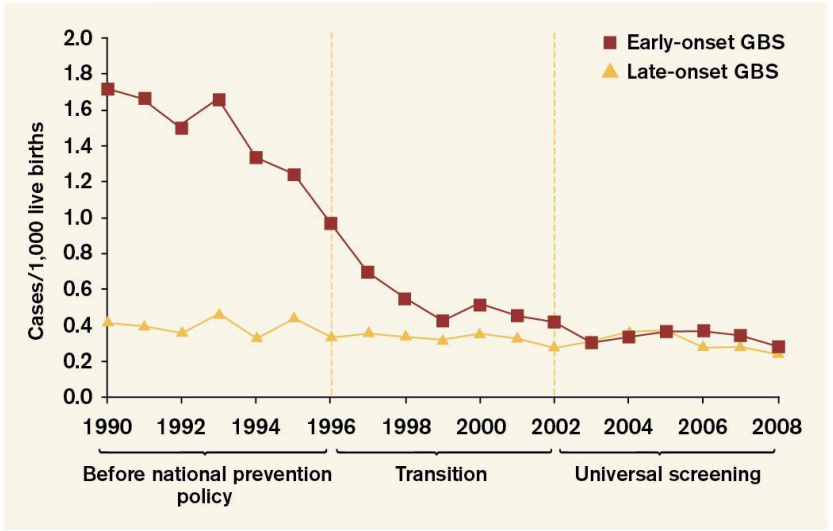
Intrapartum GBS Prophylaxis Indicated	Intrapartum GBS Prophylaxis Not Indicated
Maternal history • Previous neonate with invasive GBS disease	• Colonization with GBS during a previous pregnancy (unless colonization status in current pregnancy is unknown at onset of labor at term)
Current pregnancy • Positive GBS culture obtained at 36 0/7 weeks of gestation or more during current pregnancy (unless a cesarean birth is performed before onset of labor for a woman with intact amniotic membranes) • GBS bacteriuria during any trimester of the current pregnancy	• Negative vaginal–rectal GBS culture obtained at 36 0/7 weeks of gestation or more during the current pregnancy • Cesarean birth performed before onset of labor on a woman with intact amniotic membranes, regardless of GBS colonization status or gestational age
Intrapartum • Unknown GBS status at the onset of labor (culture not done or results unknown) and any of the following: ○ Birth at less than 37 0/7 weeks of gestation ○ Amniotic membrane rupture 18 hours or more Intrapartum temperature 100.4°F (38.0°C) or higher* ○ Intrapartum NAAT result positive for GBS ○ Intrapartum NAAT result negative but risk factors develop (ie, less than 37 0/7 weeks of gestation, amniotic membrane rupture 18 hours or more, or maternal temperature 100.4°F (38.0°C) or higher ○ Known GBS positive status in a previous pregnancy	• Negative vaginal–rectal GBS culture obtained at 36 0/7 weeks of gestation or more during the current pregnancy, regardless of intrapartum risk factors • Unknown GBS status at onset of labor, NAAT result negative and no intrapartum risk factors present (ie, less than 37 0/7 weeks of gestation, amniotic membrane rupture 18 hours or more, or maternal temperature 100.4°F (38°C) or higher

Abbreviations: GBS, group B streptococcus; NAAT, nucleic acid amplification test.

*If intraamniotic infection is suspected, broad-spectrum antibiotic therapy that includes an agent known to be active against GBS should replace GBS prophylaxis.

Modified from Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease: revised guidelines from CDC, 2010. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). MMWR Recomm Rep 2010;59(RR-10):1–36. (This Committee Opinion, including Table 1, Box 2, and Figure 1–3, updates and replaces the obstetric components of the CDC 2010 guidelines, "Prevention of Perinatal Group B Streptococcal Disease: Revised Guidelines From CDC, 2010.")

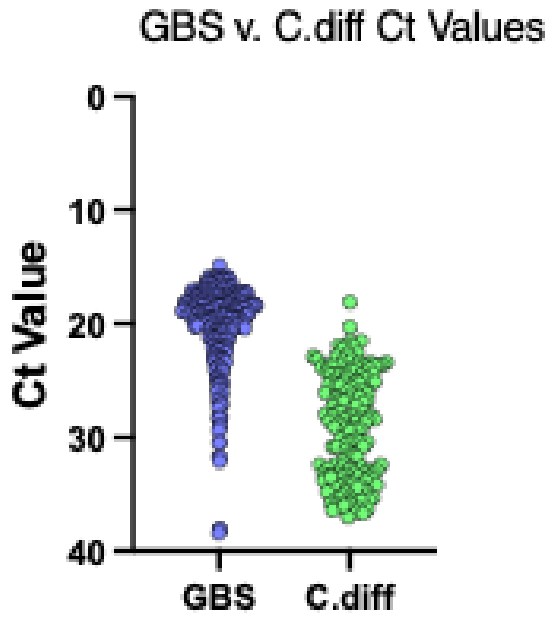
FIGURE 1 Trend of early and late-onset GBS



Incidence of early-and late-onset GBS disease in the Active Bacterial Core (ABC) surveillance areas from 1989 to 2008. The yellow line represents late-onset disease; the red line represents early-onset disease.
Source: www.cdc.gov/groupbstrep/downloads/Clinical_slideset.ppt

ACTIONS

- Cease testing per recall; transition to alternative product ASAP
- Notify laboratory leadership; escalate to hospital quality and safety
- Review testing data:
  - Determine scope of problem → 10,000s of results
  - Determine likelihood → Culture enrichment + Ct value review
- Search LIS for potentially affect patients, ordering providers
- Confirm no cases of early onset invasive GBS disease from tested patients
- ***Challenge: Linking babies to moms***



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Low probability of severe harm

COMMUNICATION REALLY IS KEY: ASSEMBLING TEAM

- Convene NBICU, Peds ID, High Risk OB / GYN
- Prepare provider communication
- Communicate with OB/GYN service line
- Communicate with NBICU and Peds
- Two primary concerns:
  - No harm in past → look back
  - How to address and track current patients
    - Had to follow current patients and babies for weeks after cessation of testing
    - 36 weeks (earlies screen) + 7 weeks (conservative 43 week delivery) + 1 week (early onset GBS)

MEMO

FROM: Yale New Haven Hospital Clinical Microbiology Laboratory

DATE: March 23, 2022

SUBJECT: Group B Streptococcus PCR Testing

Dear Obstetric Provider,

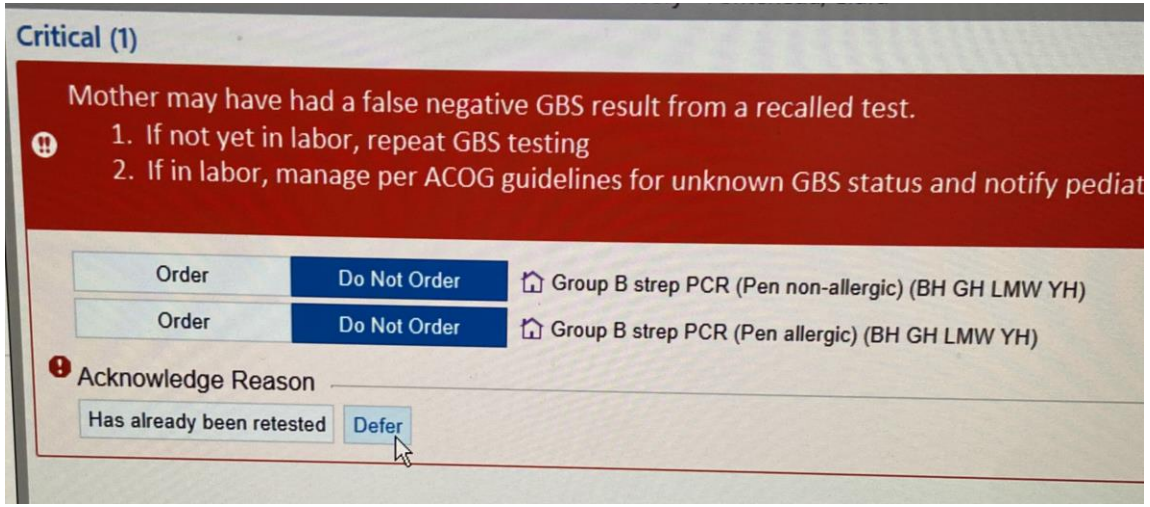
The Department of Laboratory Medicine at Yale New Haven Hospital was recently notified of a voluntary product recall from [redacted] that affects testing for Group B Streptococcus by PCR on the [redacted] instrument. [redacted] has identified a risk that this test may generate a ***false negative*** result. This risk was identified via [redacted] internal testing only and they are not aware of any patient results being affected.

Test results for Group B Streptococcus PCR generated at YNHH between 11/23/2020 and 3/18/22 may be affected. This affects only samples performed at YNHH; all samples tested at other laboratories within Yale New Haven Health are not affected, as they do not use this assay. All GBS tests that are *positive* are not affected; those patients should still be considered GBS positive.

In response to this notification:

- YNHH has stopped all testing with this method and began using a new assay on 3/18/22.
- All samples received at YNHH on or after 3/18/22, the date we were notified of a potential problem, have been tested by alternative methods and are not affected.
- Preliminary review of available laboratory and clinical data has not identified any cases of early onset invasive neonatal GBS infections associated with this testing.
- We have assessed the risk of false negative results to be very low due to the use of an additional culture enrichment step consistent with ACOG guidelines.
- We have provided a list of potentially affected patients to the clinical leadership in the Department of Pediatrics to help guide clinical decision making in the first 7 days of life for potentially affected infants.

COMMUNICATION REMAINS KEY

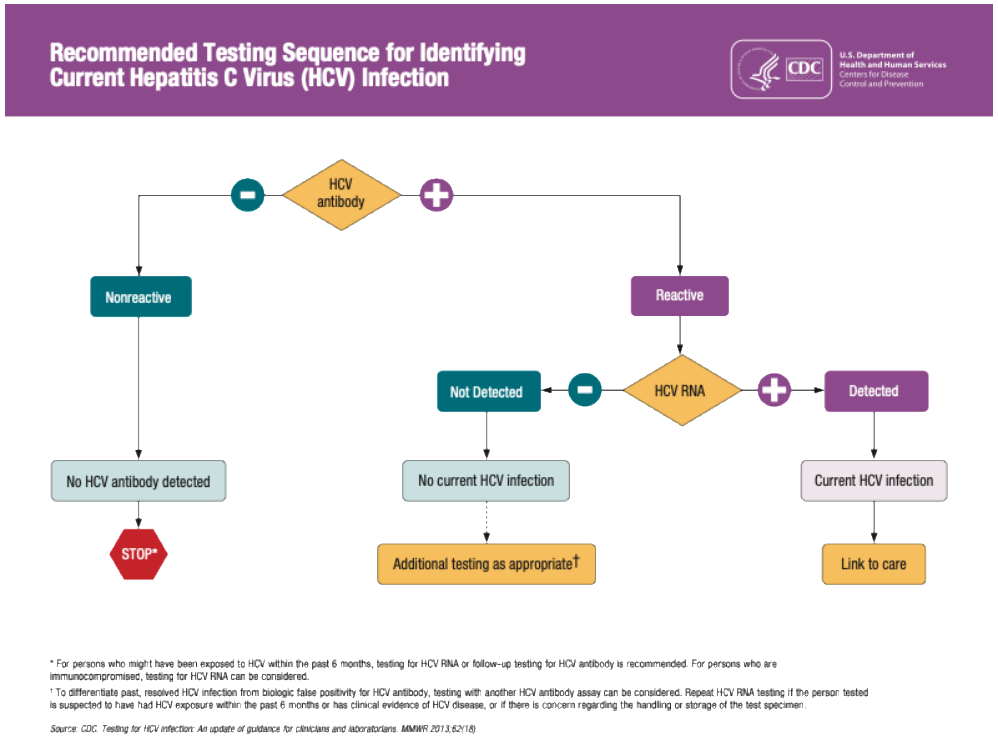


- Recommendations
- Encourage retesting when possible
- Treat as "GBS Unknown"
- Monitor outcomes until affected patients were outside window → None affected (also confirmed with vendor)
- Re-instituted assay when available again

HCV AB FOLLOWING SYPHILIS

- Customer complaints were received regarding **falsely elevated results** for some patient samples.
- Internal studies with customer return samples confirmed potential interactions that may lead to **falsely elevated results when processed as below on the same instrument**:
  - Syphilis (any result) → Anti-HCV (false pos)
  - Not restricted to same patient sample!
    - Patient A Syphilis → Patient B HCV

ROLE FOR HCV AB TESTING



- Use Cases
  - Mostly used for population screening as part of multi-step algorithm
  - 2nd line test (HCV Viral Load) unaffected
  - Can be used for acute hepatitis testing
- Potential Impact
  - Unnecessary viral load (cost?)
  - Blood donor
  - Future Immunosuppression

RISK MATRIX AND INVESTIGATIONS

	High severity	Moderate severity	Low severity
High probability	Corrective action to eliminate root cause	Corrective action to eliminate root cause	Correction of immediate problem
Moderate probability	Corrective action to eliminate root cause	Correction of immediate problem	No action necessary
Low probability	Correction of immediate problem	Correction of immediate problem	No action necessary

If the Risk Is:	Speed of Investigation	Persons Usually Involved
High	• Fast process • May need more complex actions • In-depth investigation • Time sensitive	May expand to other departments or organizations
Low	• Slower process • May need only minimal actions • Simpler investigation • Data collected and analyzed later	Laboratory

Moderate probability of low harm

OUTCOMES

Actions

- Most challenging b/c case finding not straightforward
- LIS Date / Time stamps not adequate
- Needed better definition from vendor (took a long time)
- Ultimately found likely no cases, but communicated regardless

WHAT IF THERE IS NO FIX AND THE ISSUE IS ONGOING?

- Show hands: Who has protocols in place to address know recalls with current testing (e.g. residual nucleic acid in blood culture panels, false positives in multiplex panels, AST limitations)?

- Does the error state represent an unacceptable risk for you / your lab / your institution?
- Are there reasonable (Cost? Workflow?) and effective mitigation strategies available?

WHAT CAN THE LAB DO?

- Have a (well-defined) process
  - Template and severity assessment system
  - Communication pathways and lines of responsibility
- Anticipate recalls and plan accordingly
  - Know how to pull data from instruments
  - Track lots with higher resolution

- Why are recalls so frustrating?
  - We did everything we were supposed to do, but
  - We feel we are bearing the burden to address these issues
  - Patients and providers will blame the "laboratory" with potential loss of trust and/or clients

WHAT KIND OF DETAILS DO WE NEED FROM VENDORS?

- ***We need specific details about the error state to facilitate and limit case finding***
- False positives: range of Ct values / S/CO
- Carry-over: sample-sample? Checkerboard? Within sample for multi-analyte tests? What extent? 1:100, 1:1,000, 1:100,000?
- False negatives: any guidance on narrowing? Any reproducible or predictable error states? Can we at least provide a boundary on how many affected?
- We do not know the inner workings of your instruments.
  - How they aliquot, pipet, wash, etc.
  - What samples are next to each other
  - What time frame can be considered "different batches"

VENDORS SHOULD …

Support Robust Case Finding

- Instrument software should be accessible and easily queried to quickly address and export most common recall scenarios including assay, lot, and dates.
- In a perfect world, a field representative would come on-site to extract affected cases based on company approved queries
- For more complex scenarios, vendor support is essential

Support Lab Staff

- Our staff is limited and overworked, and recalls place a large burden on them
- Vendors should have tools and resources available to help lab staff to the greatest extent possible

CONCLUSIONS

- Recalls are considered non-conforming events, but this framework doesn't perfectly apply
- All laboratories will have to deal with recalls at some point
- The severity and potential harm to patients should be the primary concern when approaching a recall.
- Current or on-going recalls may present the most critical scenarios, but older (potentially erroneous) results still may be used for clinical decision making
- Institutions have a requirement to have a process to address recalls
- There may be a range of actions taken depending on laboratory, institutional, clinical, and assay-specific factors
- There is no "one size fits all" approach