

## **Best Practices for Surveillance of Antimicrobial Resistance via Electronic Laboratory Reporting** *Recommendations from the CSTE AR/ELR Working Group, June 2017*

Many surveillance initiatives, such as monitoring new and reemerging antimicrobial resistance (e.g., Carbapenem-Resistant Enterobacteriaceae (CRE)), are conducted entirely based on laboratory observation findings and are only made possible through electronic laboratory reporting (ELR), since manual data collection processes are too resource intensive. In November 2016, CSTE convened an AR/ELR Workgroup to focus on best practices and issues related to capturing CRE in HL7 2.5.1 standard format for reporting purposes to Public Health Agencies (PHA).

The purpose of this document is to capture AR/ELR workgroup members' experience with receiving and processing CRE ELRs from laboratories and recommend related best practices for working with laboratories and CRE ELR messages. This document focuses on laboratory reporting only; reporting from providers is outside of its scope. PHAs are the primary audience for these best practices, but many recommendations are closely tied to laboratory systems and practices and may be applicable to those settings. Although the focus of the workgroup is on CRE reporting, these best practices may also be applicable to surveillance for other antimicrobial resistant organisms.

### **I. Communicating with Labs**

#### **A. State health agencies should clearly communicate with laboratories regarding reporting requirements for CRE. This communication should include:**

- Whether CRE is reportable in their jurisdiction
- Their jurisdiction's surveillance definition for CRE. Note that this may differ from clinical definitions. The current [CSTE position statement](#) definition is as follows:
  - Carbapenem-Resistant *Enterobacteriaceae* (CRE): Any organism in the *Enterobacteriaceae* family that is resistant to at least one carbapenem antibiotic (i.e. doripenem, ertapenem, imipenem, meropenem).
  - Carbapenemase-Producing Carbapenem-Resistant *Enterobacteriaceae* (CP-CRE): Any organism in the *Enterobacteriaceae* family that tests positive for carbapenemase production (e.g. KPC, VIM, NDM, IMP, OXA-48-like) by a phenotypic (e.g. CarbaNP, mCIM, modified Hodge) OR tests positive for a known carbapenemase resistance mechanism by a recognized test (e.g. PCR, Xpert Carba-R).
- When to report CRE
- How to report: see HL7 ELR Implementation Guide
- Whom to contact at the public health jurisdiction for questions regarding testing methods and reporting

Examples of written guidance for labs (See Appendix C):

- [Massachusetts](#)
- [New Mexico](#)
- [Indiana](#)

#### **B. State health agencies should also be aware of laboratory practices that may impact the quality of ELR messages for CRE. These may include:**

- *Differences among laboratories in how CRE ELR messages are triggered.* If the lab is able to automate CRE ELR messaging, this will require less work for the lab and reduce

opportunities for missed reports. However, some labs will need to trigger ELRs manually, depending on a jurisdiction's definition of CRE and its complexity.

- *Laboratory compliance with current CLSI guidelines for MIC values.* The use of outdated MIC breakpoints can affect the interpretation of test results, especially for qualitative results.
- *Suppression of certain resistance test results according to CLSI guidelines and/or clinical formularies.* This may result in missing test results for some antimicrobials of interest to PHAs or inability to identify cases and report them to PHAs.

**C. A survey of labs may be helpful to understand the test methods and breakpoints labs are using to identify CRE. Survey items may include:**

- Laboratory's knowledge of CRE reportability and plans for reporting
- Capacity to identify organisms and perform susceptibility and carbapenemase testing
- Capacity to send test results via ELR, including version of HL7 ELR messages
- Tests used to identify organisms
- Tests and MIC interpretive criteria and or zone diameter interpretive criteria used to identify antimicrobial susceptibility
- Carbapenemase confirmatory tests
- Practices for sending isolates to other labs for additional testing
- The approximate number of *Enterobacteriaceae* results produced by the laboratory during a specific time period

## II. Receiving and Processing HL7 ELR Messages

To fully assess antimicrobial resistance and categorize resistance properly, public health agencies need to receive enough information about resistance testing for specific organisms. This includes: 1) the antimicrobial/bactericidal agent being tested; 2) the method of testing (K-B, MIC, etc.); 3) the actual quantitative and qualitative results and interpretations. This information is used to monitor for multi-drug resistant organisms that require stronger antibiotics to treat infections.

Specific fields in the HL7 message allow for the CRE report (and other susceptibilities) to be reported to PHA. The message(s) used to report CRE (and other susceptibilities) should contain the organism, antibiotic susceptibilities, and the specimen source. The parent observation is the identified organism (e.g. *Klebsiella pneumoniae*) and the child observation is the antibiotic susceptibility results. The child observation should list all antibiotics tested against the organism, the measured MIC values, and the phenotypic interpretation (e.g. drug 1 ... <1 ug/mL susceptible, drug 2 ... = 2 ug/mL intermediate, drug 3 ... >= 16 ug/mL resistant).

In order to link the parent-child observations together, the child OBR should contain a *sub\_id*, sent in the child OBR 26.3, that links with the correct organism *sub\_id* located in the parent OBX 4. The child OBR should also contain the *parent filler order number* and *placer order number* located in the OBR 29.2 and OBR 29.1 that matches the parent *filler order number* and *placer order number* located in the parent OBR 3.

[http://www.hl7.org/implement/standards/product\\_brief.cfm?product\\_id=98](http://www.hl7.org/implement/standards/product_brief.cfm?product_id=98)

Simplified Example:

<b>Message Type (HL7 2.5.1)</b>
Example: <b>Multiple OBR segments</b> , has parent and child information MSH PID ORC OBR 1 OBX 1 OBX 2 SPM (such as a culture) OBR 2 (OBR-26 (Parent Result Link) and OBR-29 (Parent)) OBX 1 OBX 2 SPM (such as a bacterial isolate)
Counterexample: <b>Multiple OBR segments</b> , no parent and child information MSH PID ORC OBR 1 OBX 1 OBX 2 OBR 2 OBX 1 OBX 2

See [Appendix D](#) for additional examples of actual HL7 ELR messages for CRE. See [Appendix E](#) for additional guidance on parent-child relationships for culture and susceptibility testing.

Links to HL7 Implementation Guides:

HL7 2.5.1 for ELR is the ideal message structure for sending antimicrobial resistance messages, as it allows for the capturing of parent-child relationships in a more complete fashion than using HL7 2.3.1. Culture and susceptibility reporting is outlined in Appendix A of the R1 ELR IG.

*HL7 Version 2.5.1 Implementation Guide: Electronic Laboratory Reporting to Public Health, Release 1 (US Realm) HL7 Version 2.5.1: ORU^R01:*

[http://www.hl7.org/implement/standards/product\\_brief.cfm?product\\_id=98](http://www.hl7.org/implement/standards/product_brief.cfm?product_id=98)

Section of Parent/child, Culture and Susceptibilities should be noted.

*Errata for V251 Implementation Guide: Electronic Laboratory Reporting to Public Health (US Realm), Release 1*

[http://www.hl7.org/implement/standards/product\\_brief.cfm?product\\_id=245](http://www.hl7.org/implement/standards/product_brief.cfm?product_id=245)

*HL7 Version 2.5.1 Implementation Guide: S&I Framework Lab Results Interface, Release 1- US Realm\**

[http://www.hl7.org/implement/standards/product\\_brief.cfm?product\\_id=279](http://www.hl7.org/implement/standards/product_brief.cfm?product_id=279)

\*A newer version of this implementation guide is currently in HL7 Ballot and is expected to be published later in 2017. This newer version will actually harmonize the Lab Ordering and Lab Results interfaces and will also include profiles to support more specific lab reporting use cases, including reporting to public health. This public health profile will in effect replace, or serve as an update to the previously referenced ELR implementation guide, list above. Once published, this document will be made available at [http://www.hl7.org/implement/standards/product\\_matrix.cfm?ref=nav](http://www.hl7.org/implement/standards/product_matrix.cfm?ref=nav)

#### **A. Commonly observed deficiencies in received HL7 ELR messages:**

- 1) *No utilization of parent/child linking of susceptibility labs to the organism(s), or parent/child relationships are used incorrectly.* Without proper parent/child linkages, determining which susceptibility results go with each identified organism may be difficult without the verification of paper laboratory results. See Appendix D on parent-child guidance.
  - *Recommendation:* Make sure facilities are submitting the correct linking values and the jurisdictions have the capabilities to utilize the parent/child result to link the susceptibility test to the organism.
- 2) *Missing organism.* Organism information is needed for public health to determine new versus recurrent cases.
  - *Example:* A reference lab may test for resistance mechanism but not for the organism, so a received report may only include the mechanism report and not be linked the original organism result.
  - *Recommendation:* Organism information should be sent.
- 3) *Missing specimen information: specimen source site (SPM8), specimen type, etc.* Specimen information is needed to determine the timeframe for defining a case as new or recurrent.
  - *Recommendation:* Specimen information should be sent.
- 4) *Results are sent in NTE segments.*
  - *Recommendation:* All results should be sent in an OBX segment; quantitative results should be sent in a numeric or structured numeric segment. Qualitative results should be sent in an OBX segment, perhaps using a CE or CWE data type, using national standard vocabulary such as LOINC and/or SNOMED. NTE segments should not be used to communicate important information.
- 5) *Comments are sent in multiple result (OBX) segments.* This can result in potentially important information not being communicated to downstream systems. If the

information does come through, use of multiple OBX segments can make reading results difficult.

- *Example:* OBX|7 “identification and susceptibility,” OBX|8 “Testing to follow”
- *Recommendation:* Placing comments in NTE segments rather than OBX segments. When there are multiple OBXs, use the OBX|4 (observation sub-id) to group related OBXs

## B. Issues with LOINC and SNOMED codes

- 1) *Generic LOINC codes may be used, making it difficult for system to classify results correctly.* Culture tests where LOINC codes are used are “generic” and require SNOMED codes in order to properly classify the results to the correct condition without being done manually. Positive culture results cannot be received by systems if generic LOINC codes are used without SNOMED codes.
  - *Recommendation:* utilize standard specific LOINC and SNOMED codes that can assist in properly identifying CRE, and work with laboratory and epidemiology staff to ensure that the selected codes are correct.
    - LOINC Code look up: <https://search.loinc.org/>
    - SNOMED Code look up:  
<http://www.snomedbrowser.com/>  
<https://uts.nlm.nih.gov//snomedctBrowser.html>
- 2) *LOINC codes that do not specify the method used (e.g. disk diffusion, broth dilution/MIC, ETest, etc.)*
  - *Recommendation:* Labs should use method-specific LOINC codes.

## C. Minimum Inhibitory Concentration (MIC) values.

**Both MIC values and interpretations are needed by the PHA. MIC values are needed for trend data, which would be lost if only phenotypic interpretations are collected and the CLSI breakpoints used to determine those interpretations change over time.**

- 1) Missing MIC values
  - *Recommendation:* Use the most current CLSI guidelines (M100-S27) for MIC breakpoints, available at <http://clsi.org/m100/> (free web version).
- 2) Reference lab reporting of MIC values may be affected by their clients’ limitations, such as their willingness and ability to receive MIC values. If ordering providers are not willing or able to receive MIC values, they may not be entered in the LIMS and reference labs may not be able to send these directly to PHAs.

## D. Issues with sending laboratory’s LIM system

- 1) *Missing carbapenemase results.* Lack of carbapenemase testing results (MHT/CarbaNP, molecular panels, PCR). Facilities may be performing carbapenemase testing but not sending results to PHAs. This results in PHAs not knowing the resistance mechanism for CRE cases and needing to contact facilities to find out the testing mechanism. Some labs may report these results in comments. Reports may say “carbapenemase production” without including what tests were used to come to that conclusion, or the lab may not have run the appropriate tests.

- *Recommendation:* PHAs should understand which labs in your jurisdiction are performing these tests. If a carbapenemase test is done, labs should send results, whether positive or negative.
- 2) *Ambiguous notes/comments which may or may not indicate that carbapenemase testing was performed.* Some labs perform carbapenemase testing while others make assumptions about carbapenemase production based on overall phenotype. ELR message comments may not always make it clear whether a test was performed or not.
- *Examples:* “Demonstrates production of a carbapenemase,” “Likely carbapenemase producer”
  - *Recommendation:* PHAs should request that labs include confirmatory carbapenemase test results as “child” linkages to the “parent” organism ID. If this isn’t possible, PHAs should be aware of what carbapenemase test (if any) a lab uses, and what phenotypes trigger its use.

## Appendices:

### **A. Glossary of terms:**

Electronic Laboratory Reporting (ELR)

Public Health Agencies (PHA)

Carbapenem-Resistant Enterobacteriaceae (CRE)

Carbapenemase-Producing Carbapenem-Resistant *Enterobacteriaceae* (CP-CRE)

Minimum inhibitory concentrations (MIC)

Clinical and Laboratory Standards Institute (CLSI)

Health Level Seven (HL7)

Logical Observation Identifiers Names and Codes (LOINC)

Systematized Nomenclature of Medicine (SNOMED)

### **B. Additional resources:**

- Laboratory Protocol for Detection of Carbapenem-Resistant or Carbapenemase-Producing, *Klebsiella* spp. and *E. coli* from Rectal Swabs:  
[https://www.cdc.gov/HAI/pdfs/labSettings/Klebsiella\\_or\\_Ecoli.pdf](https://www.cdc.gov/HAI/pdfs/labSettings/Klebsiella_or_Ecoli.pdf)
- CDC technical standards resources:  
<https://www.cdc.gov/elr/technicalstandards.html>

### **C. Sample written guidance for laboratories**

- [Massachusetts](#)
- [New Mexico](#)
- [Indiana](#)

### **D. [Examples of HL7 ELR messages for CRE](#)**

### **E. [Parent/Child ELR Relationship for Culture and Susceptibility testing](#)**

## How to report Carbapenem-resistant Enterobacteriaceae to MDPH, September 2016

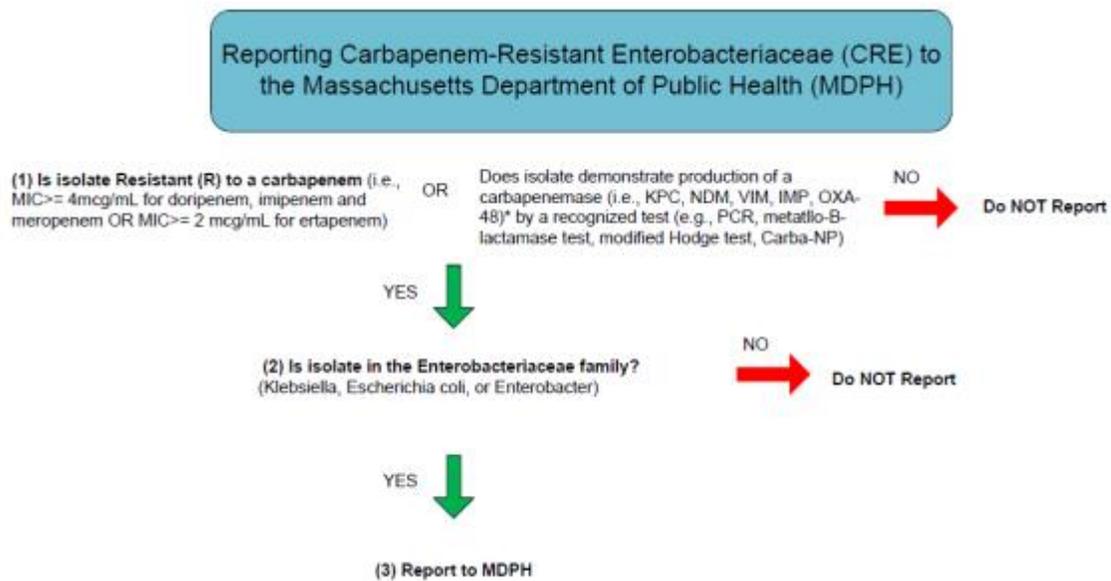
**Introduction:** Carbapenem-resistant Enterobacteriaceae (CRE) are an emerging and epidemiologically important threat. Carbapenem antibiotics are often used as the last line of treatment for infections caused by highly resistant bacteria, including those in the Enterobacteriaceae family. Increased antimicrobial resistance limits treatment options. Of increasing concern are carbapenemase-producing CRE (CP-CRE), which contain mobile resistance elements that facilitate transmission of resistance to other Enterobacteriaceae (1). Since first detection of CP-CRE in the United States in 1996 (2), CP-CRE have spread rapidly, with cases reported in 48 of 50 states (3). Infections with CP-CRE are difficult to treat and associated with high mortality rates (4). Early detection and aggressive implementation of infection prevention and control strategies are necessary to prevent further spread of CRE and CP-CRE. These strategies require an understanding of the prevalence or incidence of CRE and CP-CRE. The development and use of a standardized definition is central to this process.

The detection of and definitions for CRE are complicated. Unlike other antibiotic-resistant organisms like methicillin-resistant *Staphylococcus aureus*, which represent a single species and a single resistance mechanism, Enterobacteriaceae are a family of more than 70 organisms, and carbapenem resistance can be due to a variety of mechanisms (5). Carbapenemase production, most commonly *Klebsiella pneumoniae* carbapenemase (KPC), has been primarily responsible for the emergence of CRE in the United States over the last decade (5). For this reason, CP-CRE have become an important target for prevention. However, there is wide variability in the capacity of clinical and public health laboratories to test for carbapenemase production as the mechanism for carbapenem resistance. CRE definitions that include all isolates testing as nonsusceptible to at least one carbapenem are sensitive but might lack specificity for the most common CP-CRE currently found in the United States (KPC). Due to this limitation, certain phenotypic definitions have been developed to identify likely CP-CRE to define priorities for aggressive prevention interventions. Regardless of the definition, any organism nonsusceptible to a carbapenem may be considered a multidrug-resistant organism and warrant the use of transmission-based precautions for patients admitted to a healthcare facility (e.g., Contact Precautions).

In 2014, CDC conducted an evaluation of the 2012 CRE definition (used by the Emerging Infections Program (5) and in the 2012 CDC CRE toolkit (6)) using 312 *Escherichia coli*, *Klebsiella* spp., and *Enterobacter* spp. isolates nonsusceptible to at least one carbapenem (7). Results from these analyses demonstrated that the 2012 CDC definition misclassified 13% of carbapenem nonsusceptible *Klebsiella* spp. and 21% of KPC-producing *Klebsiella* spp. as non-CP. A CRE definition (the 2015 definition proposed here) that included isolates resistant to any carbapenem (including ertapenem) rarely missed CP strains, but captured a higher proportion of non-CP strains (55%). Adding the modified Hodge test (MHT) to this definition decreased the non-CP-CRE captured from 55% to 12%.

**Case definition:** *Enterobacter* spp., *E.coli* or *Klebsiella* spp., from any clinical specimen resistant to any carbapenem (minimum inhibitory concentrations of  $\geq 4$  mcg/ml for meropenem, imipenem, and doripenem or  $\geq 2$  mcg/ml for ertapenem) OR production of a carbapenemase (e.g., *Klebsiella pneumoniae* carbapenemase [KPC], New Delhi metallo- $\beta$ -lactamase [NDM], Verona integron-encoded metallo- $\beta$ -lactamase [VIM], imipenemase [IMP] metallo- $\beta$ -lactamase, OXA-48 carbapenemase) demonstrated by a recognized test (e.g., polymerase chain reaction, metallo- $\beta$ -lactamase test, modified Hodge test, Carba NP). Include all susceptibility results (quantitative MIC value, and qualitative interpretation (S, I, R),), plus all results regarding carbapenemase production (positive or negative).

## Appendix C: Sample written guidance for laboratories – Massachusetts



### Using the ELR portal

Go to the Organism tab and look for Multi Drug Resistant Organism in the drop-down list

Here's the description of what to report:

**Clinical Description:** Carbapenem-resistant Enterobacteriaceae (CRE) infections have many different clinical presentations. Colonization with a CRE is sometimes detected through surveillance cultures.

**What to Report:**

- Isolation of *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Enterobacter aerogenes*, or *Enterobacter cloacae* with resistance to imipenem, meropenem, doripenem, or ertapenem (from any site);
- Any isolate of *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Enterobacter aerogenes*, or *Enterobacter cloacae* that demonstrates production of a carbapenemase (e.g., KPC, NDM, VIM, IMP, OXA-48) by a recognized test (e.g., polymerase chain reaction, metallo- $\beta$ -lactamase test, modified Hodge test, Carba NP).
- Include susceptibility result values (MIC) and interpretations (S, I, R).

Here are the available test/result codes:

LOINC	LOINC NAME	SNOMED	SNOMED NAME
11475-1	Microorganism identified : PrId : Pt : xxx : Nom : Culture	112283007	Escherichia coli
		14385002	Enterobacter cloacae
		62592009	Enterobacter aerogenes
		56415008	Klebsiella pneumonia
		40886007	Klebsiella oxytoca

## Appendix C: Sample written guidance for laboratories – Massachusetts

75683-3	bla(KPC) QI Prb Mag	10828004 260385009	Positive Negative
75686-6	bla(IMP) QI Prb Mag	10828004 260385009	Positive Negative
75684-1	bla(NDM) QI Prb Mag	10828004 260385009	Positive Negative
75685-8	bla(VIM) QI Prb Mag	10828004 260385009	Positive Negative
75687-4	bla(OXA) QI Prb Mag	10828004 260385009	Positive Negative

Once you have completed your mapping, please test your mapping in the Staging site first. Send one or two test messages through and let us know; we will review them and give you the go-ahead to send them into the LIVE ELR portal.

### References

1. Gupta N, et al. Carbapenem-Resistant Enterobacteriaceae. Clin Infect Dis 2011; 53:60-67
2. Yigit H, et al. Novel Carbapenem-Hydrolyzing Beta-Lactamase, KPC-1, from a Carbapenem-Resistant Strain of *Klebsiella pneumoniae*. Antimicrob Agent Chemother 2001; 45:1151-1161
3. CDC. Carbapenemase-Producing Carbapenem-Resistant Enterobacteriaceae in the United States. Available at <http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html> . Last viewed 5 March 2015
4. Patel G, et al. Outcomes of Carbapenem-Resistant *Klebsiella pneumoniae* Infection and the Impact of Antimicrobial and Adjunctive Therapies. Infect Control Hosp Epidemiol 2008; 29:1099-1106
5. CDC. [Vital Signs: Carbapenem-Resistant Enterobacteriaceae](#). MMWR Morb Moral Wkly Rep. 2013;62:165-170
6. Centers for Disease Control and Prevention (CDC): Guidance for control of Carbapenem Resistant Enterobacteriaceae (CRE): 2012 CRE toolkit available at: <http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html>
7. Chea N, Bulens SN, Kongphet-Tran T et al An evaluation of phenotypic definitions for the identification of carbapenemase-producing carbapenem-resistant Enterobacteriaceae, United States. Emerging Infectious Diseases (in press)

## Reporting Carbapenem-resistant Enterobacteriaceae (CRE) to the New Mexico Department of Health via ELR

Interim guidance  
January 2017

### CRE Reporting guidelines

Reporting guidelines are designed to capture all cases that fit the NM-DOH CRE and CP-CRE case definition, to identify organisms with resistance and to allow NM-DOH to differentiate between CRE cases and CP-CRE cases.

**When** to Report: Laboratory isolation of **any Enterobacteriaceae genera with resistance** to imipenem, meropenem, doripenem, or ertapenem *from any site*.

Whenever an Enterobacteriaceae genera organism is tested for **resistance mechanism**.  
Any **diagnosis of Carbapenem-resistant Enterobacteriaceae (CRE)** or Carbapenamase-producing CRE (CP-CRE) infection or colonization.

**What** to Report: The **Enterobacteriaceae genera** that is resistant to carbapenamase.  
The results of all susceptibility testing done on the specimen, including MIC and interpretations  
All results (positive and negative) resistance mechanism tests (Modified Hodge Test, CarbaNP, KPC, NDM, VIM, IMP, OXA-48, etc).

Reporting regulations <https://nmhealth.org/publication/view/regulation/372/>  
<http://164.64.110.239/nmac/parts/title07/07.004.0003.htm>

For additional guidance or if any of these components cannot be reported via ELR, please contact Amy Drake ([amy.drake@state.nm.us](mailto:amy.drake@state.nm.us) or 505-827-0046).

### **Indiana State Department of Health Laboratory guidance on implementing training**

To promote enhanced detection of CP-CREs in the state of Indiana, the Indiana State Department of Health Laboratories (ISDHL) developed a series of workshops to teach the theory and practice of how to detect CP-CRE within the clinical laboratory setting. These trainings provide instruction on phenotypic and molecular methods of detection, as well as methods to assess patient colonization. By combining didactic theory with hands-on practical experience, attendees walk away with a complete training experience.

The ISDHL journey started in 2013 with a CRE Pilot Study. This pilot study was instrumental for guiding ISDHL program development and provided the data necessary to make CP-CRE reportable in Indiana. Specifically, the pilot project demonstrated that CP-CRE reporting rules should be CLSI-independent. Instead, relying on MIC- or zone diameter, a phenotypic screening recommendation, and guidelines should be written to allow for the emergence of newer technologies, such as molecular assays.

On December 25, 2015, the ISDH made CP-CRE reportable for condition, laboratory reporting, and isolate submission in Indiana. In order to facilitate awareness and enhance laboratory practices, the ISDHL developed and hosted a series of CP-CRE workshops starting in 2015. The CP-CRE workshop utilizes a pre- and post-test format to determine if knowledge gaps were addressed through the workshop materials. The workshops had three main goals: (1) understand the differences between CRE and CP-CRE and how this impacts transmission, (2) understand how to screen for CP-CRE and submit isolates to ISDHL for confirmation, and (3) teach laboratory methods for CP-CRE isolate confirmation and colonization screening.

As of May 2017, 46 microbiologists from 36 facilities have attended this workshop. When comparing pre- and post-workshop testing scores, participants scored an average of 47% higher on the post-test, indicating an increased understanding of the testing material after completing the workshop. Attending laboratories have also demonstrated a 19% increase in screening accuracy when compared with laboratories who have not yet attended, indicating workshop efficacy.

#### **Vision:**

This workshop is not just about the isolates; it's about engaging laboratorians on this emerging and evolving topic. If we've done our job, at the end of the workshop we not only have taught the students the techniques, but we've also engaged them in the problem. In general, this workshop aims to increase the level of awareness and communication between Indiana clinical laboratories and ISDHL on the topic of CP-CRE and antibiotic resistance.

#### **Goals:**

##### **1. Understand the differences between CRE and CP-CRE and how this impacts transmission**

Purpose: CP-CRE are a global threat to public health due to the mobile nature of these enzymes, which are typically encoded upon plasmids. Carbapenemases confer resistance to all  $\beta$ -lactam antibiotics, including the carbapenems, which are often considered the last

line antibiotics for Gram negative infections. Carbapenemases are mobile resistance mechanisms, and thus present an increasing threat for infection control. Understanding the differences between CRE and CP-CRE (e.g. type of resistance mechanism) is important for proper detection, containment, and prevention of these multidrug-resistant organisms. In essence, the workshop aims to answer the question: what are CP-CREs, how do they differ from CREs, and what is the impact of this from the patient and public-health level?

Resources:

- [Appendix A: Selected slides on Carbapenemase Producing – Carbapenem Resistant \*Enterobacteriaceae\*](#)

**2. Understand how to screen for CP-CRE and submit isolates to ISDHL for confirmation**

Purpose: CP-CRE is isolate reportable in Indiana. In order to meet this requirement, laboratorians need to understand how to screen for CP-CRE, what qualifies as a CP-CRE, how quickly these isolates must be submitted, and how to submit these isolates to the state public health laboratory.

One of the main components of the Indiana Communicable Disease Reporting Rule is the inclusion of a phenotypic assessment of carbapenemase production, however, ISDHL's CRE pilot identified that many laboratorians were unsure of how to perform these tests required to identify carbapenemase production. Therefore, the training aims to increase the attendee's knowledge-base on use of these methods.

For Indiana: Laboratories must submit organisms that are

- 1.) Nonsusceptible to at least one (1) carbapenem antibiotic with an MIC  $\geq 2$   $\mu\text{g/mL}$  or  $\leq 22$  mm ( $\leq 21$  mm for ertapenem) AND are positive for carbapenemase production by a phenotypic method OR
- 2.) Nonsusceptible to at least three (3) carbapenem antibiotics (with MIC  $\geq 2$   $\mu\text{g/ml}$  or zone diameter  $\leq 22$  mm ( $\leq 21$  mm for ertapenem) OR
- 3.) Positive for a carbapenemase gene maker.

These results are to be reported within 72 hours to the state health department AND the isolate must be submitted to the state laboratory for CRE characterization. Patients that are repeatedly positive with the same organism are not required to submit duplicate isolates.

Resources

- [Appendix B: How to submit isolates to state laboratory](#)
- [Appendix C: ISDH Laboratories Reporting Requirements](#)

**3. Learn some new (or old) lab methods**

Purpose: Demonstrate both new and old techniques that clinical laboratories could implement to detect carbapenemases in their laboratory.

The workshop explains the differences in testing methods for carbapenemase production. Detailed technical information on testing including the theory behind the testing methods is provided. Practical information, such as commercial availability of products, technician-time, cost-per-test, and training considerations are also provided. Limitations to the test method are discussed so that the laboratorians can be aware of potential scenarios that could cause false-positive and false-negative results and how to troubleshoot these scenarios when they occur. A hands-on bench training is then provided, allowing workshop participants to visualize the methods described in the didactic portion of the workshop.

The workshop is structured to allow for time to discuss the many barriers to test implementation, including: how to perform validations/verifications of non-FDA-approved tests and determining the cost/benefit to implementing colonization screening. Big picture concepts are also discussed, such as: how to engage the laboratory administration, how to demonstrate the savings that the laboratory can provide by decreasing the number of patient days in isolation, and the role the laboratory plays in antibiotic stewardship.

Resources

- [Appendix D: Laboratory Methods of Testing](#)
- [Modified Hodge Test \(MHT\) for Carbapenemase Detection](#)

**Appendix A: Selected slides on CP-CRE**

Carbapenemase Producing –  
Carbapenem Resistant *Enterobacteriaceae*

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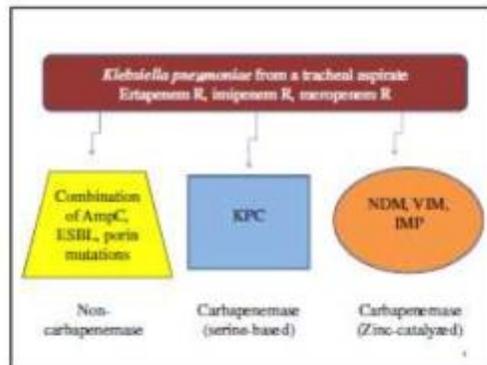
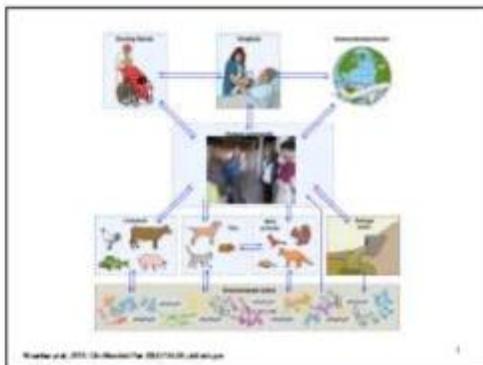
**CARBAPENEM-RESISTANT  
ENTEROBACTERIACEAE**

9,000  
600  
7,000  
1,400

NATIONAL ACTION  
PLAN FOR COMBATING  
ANTIBIOTIC-RESISTANT  
BACTERIA

Epidemiology and  
Laboratory Capacity  
Cooperative Agreement

Antibiotic Resistance Threats in the United States, 2013



What about all of these acronyms?

Organism Group	Glucose Non- Fermenters		Enterobacteriaceae	
	ESBL-test	Carbapenemase	ESBL or AmpC plus porin test	Carbapenemase
CRE	-	-	Y	Y
CP-CRE	Y	Y	Y	Y

CRE – Carbapenem Resistant *Enterobacteriaceae*  
CP-CRE – Carbapenemase Producing Carbapenem Resistant *Enterobacteriaceae*

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ISDH Epi  
Tina Feaster  
Nicole Heaton  
Df Shannon

ISDH LIMS  
Ray Beebe  
Henry Fu  
Sitha Kaliaperumal  
Carl Rothenbacher

ISDH Labs  
Judy Lovchik  
Lixia Liu\*  
Mark Glazier  
Kate Walmsright

ISDH Outreach/Training  
Shelley Matheson  
Jyl Madlem

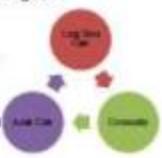
**Appendix B: How to submit an isolate sample to the state laboratory**

<b>CP-CRE (isolate)</b>	
<b>Short Name</b>	Carbapenemase Producing - Carbapenem Resistant Enterobacteriaceae
<b>Specimen Requirements</b>	<ol style="list-style-type: none"> <li>1. Specimen type: Pure viable culture on appropriate agar medium slant.</li> <li>2. One isolate per patient.</li> <li>3. ISDH Communicable Disease Rule 410-IAC 1-2.3-76 requires submission of these isolates within (3) business days of isolation.</li> <li>4. Temperature requirement: Ambient conditions.</li> </ol>
<b>Sampling Materials</b>	<ol style="list-style-type: none"> <li>1. Sample Container: Appropriate agar medium slant in tube with screw-cap tightened or other similarly approved commercial transport medium.</li> <li>2. Shipping boxes/containers with appropriate shipping labels, commercially available.</li> </ol>
<b>Procedural Notes</b>	<ol style="list-style-type: none"> <li>1. Be sure to properly label each specimen tube with the patient's name, date of birth, and date of isolation. A minimum of two unique patient identifiers are required to be present on submitted specimen.</li> <li>2. Check the expiration date on the tube to ensure the product is acceptable and will continue to be acceptable once received at the ISDH laboratory.</li> <li>3. Complete the LimsNet submission form for CRE testing. LimsNet is available on the web at <a href="http://limsnet.isdh.in.gov">http://limsnet.isdh.in.gov</a>. Users should call the lab's LIMS Help Desk to get access to this system. The Help Desk can be reached at 888-535-0011, or locally at 317-921-5506. Submitters can also email the Help Desk at <a href="mailto:LimsAppsupport@isdh.in.gov">LimsAppsupport@isdh.in.gov</a>.</li> </ol>
<b>Shipping Instructions</b>	<p>Ship To: Indiana State Department of Health Laboratories 550 West 16th Street Indianapolis, IN 46202</p> <ol style="list-style-type: none"> <li>1. Package according to Category B UN3373 triple contained in accordance with federal shipping regulations for infectious substances/diagnostic specimens.</li> <li>2. Tighten the specimen container tube caps.</li> <li>3. Label clearly on each specimen tube with the patient name, date of birth, and date of isolation.</li> <li>4. Wrap each labeled, primary/specimen container tube with absorbent material. Place each primary container tube with absorbent material into the inner mailing container and tighten the cap securely.</li> <li>5. The completed submission/request form may then be wrapped around the sealed inner container and together placed securely into the outer shipping container.</li> <li>6. Clearly label the outer container with the senders name/address and recipients name/address.</li> <li>7. Do not send culture isolates on petri plates if submitting by mail.</li> <li>8. Transport Temperature: Ambient conditions.</li> </ol>
<b>Reporting and TAT</b>	<ol style="list-style-type: none"> <li>1. Reporting Method: LimsNet</li> <li>2. TAT (ISDH Testing): 2 business days.</li> <li>3. Test Referral. Cultures identified as possible carbapenemase producing isolates with unusual profiles will be sent to the CDC for confirmation and/or further testing. Projected TAT listed above does not account for time required for isolate submission to the CDC.</li> </ol>
<b>Lab</b>	Clinical Microbiology
<b>Keywords</b>	CP-CRE, Carbapenemase Producing - CRE
<b>Fee, if applicable</b>	Not applicable.

**Appendix C: ISDH Laboratories Reporting Requirements (selected slides)**

**In Indiana, CP-CRE is reportable for both isolates and condition.**

- CDR Modification Highlights Actionable Interventions
- Sets a timeline (72 hours) for investigation
- Puts a focus on acute care and long term care
- Prevent spread by encouraging:
  - Contact precautions
  - CDC CRE Toolkit Use
  - Screening for colonization
  - Chlorhexidine bathing



Based on the potential for transmissibility, the Communicable Disease rule focuses on CP-CRE.

In order to narrow the amount of isolates required to submit to the state, the following isolate submission criteria were adopted:

Isolates include organisms that are non-susceptible to at least one carbapenem antibiotic = ab MIC  $\geq 2 \mu\text{g/ml}$  or zone diameter  $\leq 22 \text{ mm}$  ( $\leq 21 \text{ mm}$  for enterobacterales)

AND one of the following criteria:

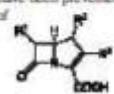
1. Are positive for carbapenemase production by a phenotypic test (e.g. Modified Hodge, or Carba NP)
2. Are non-susceptible to at least three carbapenem antibiotics with MIC  $\geq 2 \mu\text{g/ml}$  or zone diameter  $\leq 22 \text{ mm}$  ( $\leq 21 \text{ mm}$  for enterobacterales)
3. Are positive for a carbapenemase gene marker.

Only one isolate that meets these criteria should be submitted if the same organism is repeatedly recovered from the same patient.

**AST-based Review and Reporting: A Data-Driven Decision**

Review of unnecessary submissions from 2013-2015:

- 98.8% of these submissions could have been prevented with the CDR algorithm:
  - 55.6% by specifying the MIC or Zone Diameter
  - 43.2% by assessing phenotypic carbapenemase production
- Only 38% of these submissions would have been prevented with an alternative submission criteria of resistance to only 2 carbapenems



Structure of carbapenem antibiotics, wikipedia.org

**Three day submission criteria ...**

- (1) CP-CRE
- (2) Haemophilus influenzae, invasive disease.
- (3) Neisseria meningitidis, invasive disease.
- (4) STEC
- (5) VRSA
- (6) Mycobacterium tuberculosis
- (7) S. pneumoniae invasive disease ( $< 5 \text{ y.o.}$ )
- (8) Listeria monocytogenes (sterile sites)
- (9) Salmonella sp. (clinical specimen)
- (10) Shigella sp. (clinical specimen)
- (11) Vibrio cholerae (stool or vomit)
- (12) Vibrio sp. (clinical specimen)

**Day 1 – Receive isolate and subculture**

**Day 2\* – Confirms ID and Performs PCR**

- MALDI-TOF MS
- Multiplex PCR (KPC, NDM-1, OXA-48, IMP, VIM)

If Positive, report Finalized result  
 + Ex. *Klebsiella pneumoniae*, KPC positive  
 If Negative – report Preliminary Negative

**Day 3 – CarbaNP on PCR negative specimens**

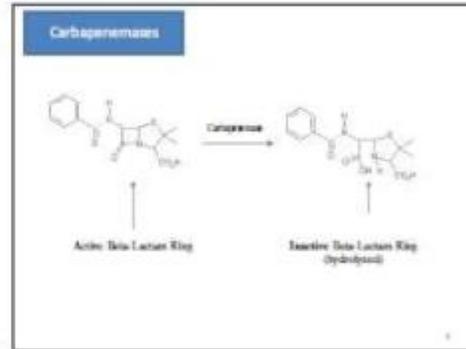
If Positive, send to CDC for further testing  
 If Negative, report out as Negative

**ISDH Algorithm**

**Appendix D: Laboratory Methods of Testing (selected slides)**

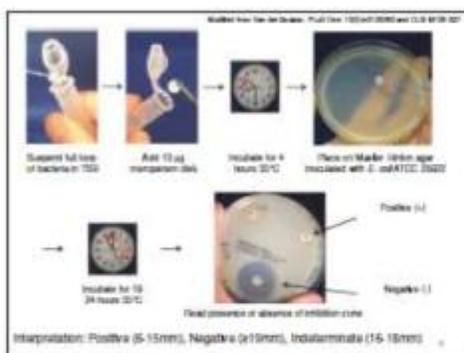
**Other Methods of Carbapenemase Detection: An Overview**

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 Indiana State Department of Health  
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 317-821-3904



**Modified Carbapenemase Inhibition Method (mCIM)**

- Basic Principle of mCIM**
- 1.) Gather materials (swabs, reagents, tubes, plates).
  - 2.) Prepare a suspension of the test organism.
  - 3.) Add a meropenem disk to the suspension. Incubate for 4 hours, 35°C, ambient air.
  - 4.) Prepare a 0.5 McFarland Solution of the *E. coli* carbapenem-susceptible strain (ATCC 25922).
  - 5.) Inoculate plate and allow to dry.
  - 6.) Remove the meropenem disk and place the in the middle of the prepared plate.
  - 7.) Incubate at 35°C, ambient air, 18 hours to overnight.
  - 8.) Inspect plate and interpret.



- Testing Details – mCIM**
- **Cost of Test:** ~\$1.00 (@ ISDH)
  - **Kit Shelf Life:** ~2-3 months (Mueller-Hinton plate)
  - **Time to Test:** 18-24 hours
  - **Hands on Time:** ~20 minutes
  - **Additional Materials:** Mueller Hinton plate, meropenem disk, Tweezers/Forceps, alcohol pad, McFarland standard/turbidity meter, cotton swabs, tubed saline, control organisms



## Appendix D: Example HL7 ELR Messages

### Sample HL7 2.3.1 ELR for CRE

```
1 MSH|^~\&|SENDER_CDR-ENS-MIC^|City-22D0000001-CLIA|ELR|DPH|201702230907||ORU-R01|201702230858City|P12.3.1
2 PID|1||97198121-^City||LastName-FirstName^||19870105|F||^CDCREC^--L|00 4TH AVE--BOSTON-MA-02111-UNITED STATES||^-----L|||||N
3 NK1|1|^-----
4 ORC|RE|||||City Hospital-L^-----22D0000001|10 Melville Street--Boston-MA-02115-USA||^-----617-0001000|10 Melville Street-Suite A-Boston-MA-02115-USA
5 OBR|1|AAH20004025_20170223071800-City-L|169321-CDR-L|UC-URINE CULTURE-L-630-4--LN||201702230600|||||201702230717|$$$
Urine|1043260873-ProviderLastName-ProviderMiddleName-ProviderFirstName-MD-^-----NPI|^-----617-0001000|||||201702230723||F||UC-URINE CULTURE-L-630-4--LN
6 NTE|1|RE|TEST FOR CDR|
7 NTE|1|L|URINE|RE
8 OBX|1|CE|^--11475-1-Microorganism identified : PrId : Pt : xxx : Nom : Culture-LN||^--409800005-ESCHERICHIA COLI ESBL-SCT|||||F||201702230723|22D0000001
9 NTE|1|L|>100,000 colony forming units per ml|RE
10 OBR|2|AAH20004025_20170223071800-City-L|169321-CDR-L|VITEK MIC-VITEK MIC-L-50545-3-BACTERIA SUSCEPTIBILITY-LN||201702230600|||||$$$
Urine|||||201702230723||F|$$$11475-1$$$L^--409800005||AAH20004025_20170223071800-City-169321-CDR|||||UC-URINE CULTURE-L-630-4-Bacteria identified in Urine by Culture-LN
11 OBX|1|SN|AMK-amikacin-L-18860-7-Amikacin Susc-LN|1|^0.1|MM-Millimeter-UCUM|Not Available|S||F||201702230723|22D0000001
12 OBX|2|SN|AUG-amoxicillin/clavulanate-L-18862-3-Amoxicillin+Clav Susc-LN|1|^0.5|MM-Millimeter-UCUM|Not Available|S||F||201702230723|22D0000001
13 OBX|3|SN|AMP-ampicillin-L-18864-9-Ampicillin Susc-LN|1|^16|MM-Millimeter-UCUM|Not Available|I||F||201702230723|22D0000001
14 OBX|4|SN|CZLU-cefazolin (urine)-L-16566-2-Cefazolin (urine)-LN|1|^1|MM-Millimeter-UCUM|Not Available|S||F||201702230723|22D0000001
15 OBX|5|SN|FEP-cefepime-L-18879-7-Cefepime Susc-LN|1|^1|MM-Millimeter-UCUM|Not Available|S||F||201702230723|22D0000001
16 OBX|6|SN|FOX-cefoxitin-L-18888-8-Cefoxitin Susc-LN|1|^16|MM-Millimeter-UCUM|Not Available|I||F||201702230723|22D0000001
17 OBX|7|SN|CTI-ceftazidime-L-18893-8-Ceftazidime Susc-LN|1|^1|MM-Millimeter-UCUM|Not Available|S||F||201702230723|22D0000001
18 OBX|8|SN|CRO-ceftriaxone-L-18895-3-Ceftriaxone Susc-LN|1|^1|MM-Millimeter-UCUM|Not Available|S||F||201702230723|22D0000001
19 OBX|9|SN|CIP-ciprofloxacin-L-18906-8-Ciprofloxacin Susc-LN|1|^0.5|MM-Millimeter-UCUM|Not Available|S||F||201702230723|22D0000001
20 OBX|10|SN|ERT-ertapenem-L-35802-8-Ertapenem Susc-LN|1|^8|MM-Millimeter-UCUM|Not Available|R||F||201702230723|22D0000001
21 OBX|11|SN|GEN-gentamicin-L-18928-2-Gentamicin Susc-LN|1|^0.5|MM-Millimeter-UCUM|Not Available|S||F||201702230723|22D0000001
22 OBX|12|SN|LVX-levofloxacin-L-20629-2-L-Floxacin Susc-LN|1|^0.5|MM-Millimeter-UCUM|Not Available|S||F||201702230723|22D0000001
23 OBX|13|SN|FUR-nitrofurantoin-L-18955-5-Nitrofurantoin Susc-LN|1|^64|MM-Millimeter-UCUM|Not Available|I||F||201702230723|22D0000001
24 OBX|14|SN|TZP-piperacillin/tazobactam-L-18970-4-Piperacillin+Tazobac-LN|1|^0.5|MM-Millimeter-UCUM|Not Available|S||F||201702230723|22D0000001
25 OBX|15|SN|TET-tetracycline-L-18993-6-Tetracycline Susc-LN|1|^1|MM-Millimeter-UCUM|Not Available|S||F||201702230723|22D0000001
26 OBX|16|SN|TOB-tobramycin-L-18996-9-Tobramycin Susc-LN|1|^1|MM-Millimeter-UCUM|Not Available|S||F||201702230723|22D0000001
27 OBX|17|SN|TRI-trimethoprim/sulfamethoxazole-L-18998-5-TMP SMX Susc-LN|1|^20|MM-Millimeter-UCUM|Not Available|S||F||201702230723|22D0000001
28
```



Parent/Child ELR Relationship for Culture and Susceptibility testing

**Background:** The use of a parent/child relationships is to link together child sensitivity results to the parent culture results. This is important in public health surveillance to determine the resistance of organisms to different types of medications. These results are used to monitor for super-bugs that require stronger antibiotics to treat simple infections.

In HL7 2.5.1 structure, this can be done in the observation request (OBR) segment of the HL7 message by linking the parent filler order number located in OBR 3 to the child Parent sequence located in OBR 29.2 (See example below with segments highlighted).

```
MSH|^~\&|NIST^2.16.840.1.113883.3.72.5.20^ISO|NIST^2.16.840.1.113883.3.72.5.21^ISO|NIST^2.16.840.1.1138
83.3.72.5.22^ISO|NIST^2.16.840.1.113883.3.72.5.23^ISO|20120821140551-0500||ORU^R01^ORU_R01|NIST-ELR-
004.01|T|2.5.1|||NE|NE|||PHLabReport-NoAck^HL7^2.16.840.1.113883.9.11^ISO
SFT|NIST Lab, Inc.^L^NIST&2.16.840.1.113883.3.987.1&ISO^XX^123544|3.6.23|A-1 Lab System|6742873-
12||20100617
PID|1||PATID1234^^&2.16.840.1.113883.3.72.5.24&ISO^MR^Seminole Cnty Hlth
C&2.16.840.1.113883.3.0&ISO||Jones^William^A^^L||19610615|M||2106-3^White^CDCREC|1955 Seminole
Lane^^Oveido^FL^32765^USA^H^^12059||^PRN^PH^^1^407^2351234|||N^Not Hispanic or
Latino^HL70189^NL^not latino^L^2.5.1
ORC|RE|ORD723222-4^^2.16.840.1.113883.3.72.5.24^ISO|R-783274-
4^LIS^2.16.840.1.113883.3.72.5.25^ISO|||57422^RADON^NICHOLAS^^Dr.^NPI&2.16.840.1.113883.4.6
&ISO^L^^NPI|^PRN^PH^^407^2341212|||Seminole County Health Clinic|555 Orange
Ave^^Oviedo^FL^32765^^B|^WPN^PH^^813^8847284|555 Orange Ave^^Oviedo^FL^32765^^B
OBR|1|ORD723222-4^^2.16.840.1.113883.3.72.5.24^ISO|R-783274-4^LIS^2.16.840.1.113883.3.72.5.25^ISO|625-
4^Bacteria identified in Stool by Culture^LN^3456543^CULTURE
STOOL^99USI^2.40||20110528|||57422^RADON^NICHOLAS^^Dr.^NPI&2.16.840.1.113883.4.6&ISO^L
^^NPI|^PRN^PH^^407^2341212|||201106010900-0500||F
OBX|1|CWE|625-4^Bacteria identified in Stool by Culture^LN^Bacteria identified^Bacteria
identified^99USI^2.40|1|85729005^Shigella flexneri^SCT^^^Shigella
flexneri|||F||20110528|||20110531130655-0500||Seminole County Health Department
Laboratory^^&2.16.840.1.113883.3.72.5.30.1&ISO^XX^^987|6756 Florida
Avenue^^Oveido^FL^32765^^B|10092^Pafford^Hamlin^^&2.16.840.1.113883.3.72.5.30.1&ISO^L^^NPI
SPM|1|^ORD723222-4&&2.16.840.1.113883.3.72.5.24&ISO||119339001^Stool
specimen^SCT^^^07/31/2012|||20110528|20110529
OBR|2||R-783274-5^LIS^2.16.840.1.113883.3.72.5.25^ISO|50545-3^Bacterial susceptibility panel in Isolate by
Minimum inhibitory concentration (MIC)^LN^Bact suscept^Bacteria
susceptibility^99USI^2.40||20110528|||57422^RADON^NICHOLAS^^Dr.^NPI&2.16.840.1.113883.4.6
&ISO^L^^NPI|^PRN^PH^^407^2341212|||201106010900-0500||F|625-4&Bacteria identified in Stool by
Culture&LN&Bacteria identified&Bacteria identified&99USI^^Shigella flexneri||^R-783274
4&LIS&2.16.840.1.113883.3.72.5.25&ISO
OBX|1|SN|20-8^Amoxicillin+Clavulanate [Susceptibility] by Minimum inhibitory concentration
(MIC)^LN^AmoxClav^Amoxicillin-clavulanic acid^99USI^2.40||=^16|ug/mL^microgram per
milliliter^UCUM^^^1.8.2||^Intermediate^HL70078^^^2.5.1||F||20110528|||201106010900-
0500||Seminole County Health Department
Laboratory^^&2.16.840.1.113883.3.72.5.30.1&ISO^XX^^987|6756 Florida
Avenue^^Oveido^FL^32765^^B|10092^Pafford^Hamlin^^&2.16.840.1.113883.3.72.5.30.1&ISO^L^^NPI
OBX|2|SN|516-5^Trimethoprim+Sulfamethoxazole [Susceptibility] by Minimum inhibitory concentration
```

## Appendix E: Parent/Child ELR Relationship for Culture and Susceptibility testing

(MIC)^LN^TMP-SMX^Trimethoprim-sulfamethoxazole^99USI^2.40| |=^8/^152|ug/mL^microgram per milliliter^UCUM^^^1.8.2| |R^Resistant^HL70078^^^2.5.1| |F| |20110528| | |201106010900-0500| | |Seminole County Health Department Laboratory^^^&2.16.840.1.113883.3.72.5.30.1&ISO^XX^^987|6756 Florida Avenue^^Oveido^FL^32765^^B|10092^Pafford^Hamlin^^^&2.16.840.1.113883.3.72.5.30.1&ISO^L^^NPI OBX|3|SN|185-9^Ciprofloxacin [Susceptibility] by Minimum inhibitory concentration (MIC)^LN^CIPROFLOXACIN^CIPROFLOXACIN^99USI^2.40| |<=^0.06|ug/mL^microgram per milliliter^UCUM^^^1.8.2| |S^Susceptible^HL70078^^^2.5.1| |F| |20110528| | |201106010900-0500| | |Seminole County Health Department Laboratory^^^&2.16.840.1.113883.3.72.5.30.1&ISO^XX^^987|6756 Florida Avenue^^Oveido^FL^32765^^B|10092^Pafford^Hamlin^^^&2.16.840.1.113883.3.72.5.30.1&ISO^L^^NPI

When a culture grows more than one organisms, the message sent may contain multiple susceptibility (child) results, one susceptibility result group for each organism. To make sure the child results successfully link to the correct parent results, the child OBR segment should contain a sub\_id, sent in the Parent Result sequence located in OBR 26.2, that links with the correct organism sub\_id located in the parent result's OBX 4 segment, sub\_id (see example below with segments highlighted in green).

MSH|^&|NIST^2.16.840.1.113883.3.72.5.20^ISO|NIST^2.16.840.1.113883.3.72.5.21^ISO|NIST^2.16.840.1.113883.3.72.5.22^ISO|NIST^2.16.840.1.113883.3.72.5.23^ISO|20120821140551-0500| |ORU^R01^ORU\_R01|NIST-ELR-004.01|T|2.5.1| |NE|NE| | |PHLabReport-NoAck^HL7^2.16.840.1.113883.9.11^ISO SFT|NIST Lab, Inc.^L^^NIST&2.16.840.1.113883.3.987.1&ISO^XX^^123544|3.6.23|A-1 Lab System|6742873-12| |20100617 PID|1| |PATID1234^^&2.16.840.1.113883.3.72.5.24&ISO^MR^Seminole Cnty Hlth C&2.16.840.1.113883.3.0&ISO| |Jones^William^A^^L| |19610615|M| |2106-3^White^CDCREC|1955 Seminole Lane^^Oveido^FL^32765^USA^H^^12059| |^PRN^PH^^1^407^2351234| | | |N^Not Hispanic or Latino^HL70189^NL^not latino^L^2.5.1 ORC|RE|ORD723222-4^^2.16.840.1.113883.3.72.5.24^ISO|R-783274-4^LIS^2.16.840.1.113883.3.72.5.25^ISO| | | |57422^RADON^NICHOLAS^^Dr.^NPI&2.16.840.1.113883.4.6 &ISO^L^^NPI| |^PRN^PH^^407^2341212| | | |Seminole County Health Clinic|555 Orange Ave^^Oviedo^FL^32765^^B|^WPN^PH^^813^8847284|555 Orange Ave^^Oviedo^FL^32765^^B OBR|1|ORD723222-4^^2.16.840.1.113883.3.72.5.24^ISO|R-783274-4^LIS^2.16.840.1.113883.3.72.5.25^ISO|625-4^Bacteria identified in Stool by Culture^LN^3456543^CULTURE STOOL^99USI^2.40| |20110528| | | |57422^RADON^NICHOLAS^^Dr.^NPI&2.16.840.1.113883.4.6&ISO^L^^NPI|^PRN^PH^^407^2341212| | | |201106010900-0500| |F OBX|1|CWE|625-4^Bacteria identified in Stool by Culture^LN^Bacteria identified^Bacteria identified^99USI^2.40| |85729005^Shigella flexneri^SCT^^^Shigella flexneri| | | |F| |20110528| | |20110531130655-0500| | |Seminole County Health Department Laboratory^^^&2.16.840.1.113883.3.72.5.30.1&ISO^XX^^987|6756 Florida Avenue^^Oveido^FL^32765^^B|10092^Pafford^Hamlin^^^&2.16.840.1.113883.3.72.5.30.1&ISO^L^^NPI

## Appendix E: Parent/Child ELR Relationship for Culture and Susceptibility testing

OBX|1|CWE|625-4^Bacteria identified in Stool by Culture^LN^Bacteria identified^Bacteria identified^99USI^2.40|2|66543000^Campylobacter jejuni^SCT^^^^^Campylobacter jejuni|||||F|||20110528|||20110531130655-0500|||Seminole County Health Department Laboratory^^^^&2.16.840.1.113883.3.72.5.30.1&ISO^XX^^^987|6756 Florida Avenue^^Oveido^FL^32765^^B|10092^Pafford^Hamlin^^^^^^&2.16.840.1.113883.3.72.5.30.1&ISO^L^^^NPI SPM|1|^ORD723222-4&&2.16.840.1.113883.3.72.5.24&ISO||119339001^Stool specimen^SCT^^^^07/31/2012|||||||20110528|20110529

OBR|2||R-783274-5^LIS^2.16.840.1.113883.3.72.5.25^ISO|50545-3^Bacterial susceptibility panel in Isolate by Minimum inhibitory concentration (MIC)^LN^Bact suscept^Bacteria susceptibility^99USI^2.40|||20110528||||||57422^RADON^NICHOLAS^^^Dr.^^^NPI&2.16.840.1.113883.4.6 &ISO^L^^^NPI|^PRN^PH^^407^2341212|||||201106010900-0500|||F|625-4&Bacteria identified in Stool by Culture&LN&Bacteria identified&Bacteria identified&99USI^1^Shigella flexneri|||^R-783274-4&LIS&2.16.840.1.113883.3.72.5.25&ISO

OBX|1|SN|20-8^Amoxicillin+Clavulanate [Susceptibility] by Minimum inhibitory concentration (MIC)^LN^AmoxClav^Amoxicillin-clavulanic acid^99USI^2.40||=^16|ug/mL^microgram per milliliter^UCUM^^^^1.8.2|||^Intermediate^HL70078^^^^2.5.1|||F|||20110528|||||201106010900-0500|||Seminole County Health Department Laboratory^^^^&2.16.840.1.113883.3.72.5.30.1&ISO^XX^^^987|6756 Florida Avenue^^Oveido^FL^32765^^B|10092^Pafford^Hamlin^^^^^^&2.16.840.1.113883.3.72.5.30.1&ISO^L^^^NPI

OBX|2|SN|516-5^Trimethoprim+Sulfamethoxazole [Susceptibility] by Minimum inhibitory concentration (MIC)^LN^TMP-SMX^Trimethoprim-sulfamethoxazole^99USI^2.40||=^8/^152|ug/mL^microgram per milliliter^UCUM^^^^1.8.2|||^Resistant^HL70078^^^^2.5.1|||F|||20110528|||||201106010900-0500|||Seminole County Health Department Laboratory^^^^&2.16.840.1.113883.3.72.5.30.1&ISO^XX^^^987|6756 Florida Avenue^^Oveido^FL^32765^^B|10092^Pafford^Hamlin^^^^^^&2.16.840.1.113883.3.72.5.30.1&ISO^L^^^NPI

OBX|3|SN|185-9^Ciprofloxacin [Susceptibility] by Minimum inhibitory concentration (MIC)^LN^CIPROFLOXACIN^CIPROFLOXACIN^99USI^2.40||<=^0.06|ug/mL^microgram per milliliter^UCUM^^^^1.8.2|||^Susceptible^HL70078^^^^2.5.1|||F|||20110528|||||201106010900-0500|||Seminole County Health Department Laboratory^^^^&2.16.840.1.113883.3.72.5.30.1&ISO^XX^^^987|6756 Florida Avenue^^Oveido^FL^32765^^B|10092^Pafford^Hamlin^^^^^^&2.16.840.1.113883.3.72.5.30.1&ISO^L^^^NPI

OBR|2||R-783274-5^LIS^2.16.840.1.113883.3.72.5.25^ISO|50545-3^Bacterial susceptibility panel in Isolate by Minimum inhibitory concentration (MIC)^LN^Bact suscept^Bacteria susceptibility^99USI^2.40|||20110528||||||57422^RADON^NICHOLAS^^^Dr.^^^NPI&2.16.840.1.113883.4.6 &ISO^L^^^NPI|^PRN^PH^^407^2341212|||||201106010900-0500|||F|625-4&Bacteria identified in Stool by Culture&LN&Bacteria identified&Bacteria identified&99USI^2^Campylobacter jejuni|||^R-783274-4&LIS&2.16.840.1.113883.3.72.5.25&ISO

OBX|1|SN|20-8^Amoxicillin+Clavulanate [Susceptibility] by Minimum inhibitory concentration (MIC)^LN^AmoxClav^Amoxicillin-clavulanic acid^99USI^2.40||>=^32|ug/mL^microgram per milliliter^UCUM^^^^1.8.2|||^Resistant^HL70078^^^^2.5.1|||F|||20110528|||||201106010900-0500|||Seminole County Health Department Laboratory^^^^&2.16.840.1.113883.3.72.5.30.1&ISO^XX^^^987|6756 Florida Avenue^^Oveido^FL^32765^^B|10092^Pafford^Hamlin^^^^^^&2.16.840.1.113883.3.72.5.30.1&ISO^L^^^NPI

OBX|2|SN|516-5^Trimethoprim+Sulfamethoxazole [Susceptibility] by Minimum inhibitory concentration (MIC)^LN^TMP-SMX^Trimethoprim-sulfamethoxazole^99USI^2.40||=^8/^152|ug/mL^microgram per milliliter^UCUM^^^^1.8.2|||^Resistant^HL70078^^^^2.5.1|||F|||20110528|||||201106010900-0500|||Seminole County Health Department Laboratory^^^^&2.16.840.1.113883.3.72.5.30.1&ISO^XX^^^987|6756 Florida

## Appendix E: Parent/Child ELR Relationship for Culture and Susceptibility testing

Avenue^^Oveido^FL^32765^^B|10092^Pafford^Hamlin^^^^^^&2.16.840.1.113883.3.72.5.30.1&ISO^L^^^NPI  
OBX|3|SN|185-9^Ciprofloxacin [Susceptibility] by Minimum inhibitory concentration  
(MIC)^LN^CIPROFLOXACIN^CIPROFLOXACIN^99USI^2.40|<=^0.25|ug/mL^microgram per  
milliliter^UCUM^^^^1.8.2|S^Susceptible^HL70078^^^^2.5.1||F|||20110528|||201106010900-  
0500|||Seminole County Health Department  
Laboratory^^^^&2.16.840.1.113883.3.72.5.30.1&ISO^XX^^^987|6756 Florida  
Avenue^^Oveido^FL^32765^^B|10092^Pafford^Hamlin^^^^^^&2.16.840.1.113883.3.72.5.30.1&ISO^L^^^NPI