

# WEST VIRGINIA CARBAPENEM-RESISTANT ENTEROBACTERIACEAE (CRE) SURVEILLANCE REPORT

January 1, 2016—December 31, 2016

## INTRODUCTION

*Enterobacteriaceae* are a family of bacteria that commonly colonize the human digestive tract. These organisms are capable of causing a wide range of infections, including urinary tract infections, blood infections and sepsis, respiratory infections, and wound infections. Carbapenem-resistant *Enterobacteriaceae* (CRE) are organisms in this family that have developed resistance to a last line antibiotic class, the carbapenems. Infections with these organisms are often extremely difficult to treat and are associated with a high mortality rate, up to 50% in some studies.<sup>1</sup> Carbapenem resistance is spreading, making surveillance of CRE an important aspect of prevention and control efforts.

Since August 2013, laboratories testing specimens from West Virginia residents have been required to report cases of CRE to the local health department of the patient's county of residence within 1 week of detection (see 64CSR7 <http://apps.sos.wv.gov/adlaw/csr/readfile.aspx?DocId=25071&Format=PDF>). The following surveillance report summarizes data from CRE cases between January 1, 2016 and December 31, 2016.

## METHODS

For 2016 surveillance purposes, a case of CRE was defined as an *Enterobacteriaceae* isolate that is resistant to at least 1 carbapenem antibiotic OR a documented carbapenemase producer. There are 4 exceptions to this case definition: *Proteus* spp., *Providencia* spp., *Morganella* spp., and *Stenotrophomonas* spp. These organisms are intrinsically resistant to imipenem, and must be resistant to 1 carbapenem other than imipenem OR be a documented carbapenemase producer.

In previous years, a case of CRE had been classified as a case if the organism was an *Enterobacteriaceae* that was nonsusceptible to 1 of the following carbapenems: doripenem, meropenem, or imipenem and resistant to all of the following third-generation cephalosporins that were tested: ceftriaxone, cefotaxime, and ceftazidime. In 2015, the Centers for Disease Control and Prevention (CDC) adjusted its surveillance case definition in order to alleviate some confusion, and to catch any potentially missed carbapenemase producing organisms. West Virginia adjusted its case definition to align with that suggested by the CDC for 2016.

Two types of cultures are described, clinical and surveillance. Clinical cultures were taken in an effort to diagnose active infection, and surveillance cultures were rectal or fecal cultures taken to establish whether or not a patient was colonized with CRE.

Case counts are based on date of report. Each individual case is only counted 1 time regardless of how many lab results are received for each individual, the exception being a single individual reported as infected or colonized with more than 1 type of CRE organism.

The data were analyzed 2 ways: at the organism level (see Organism data) and at the patient level (see Demographics). Data were analyzed at the state, county, and regional levels. Variables with 0-4 cases are indicated with a value of "<5" in order to protect patient confidentiality. When variables have missing data, the number of cases included in the analysis is noted beside the variable name.

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<sup>1</sup> CDC, 2012 CRE Toolkit - Guidance for Control of Carbapenem-resistant *Enterobacteriaceae* (CRE)

As per the West Virginia Department of Health and Human Resources (DHHR), Bureau for Public Health, Division of Infectious Disease Epidemiology CRE Notification Protocol,<sup>2</sup> local health departments are expected to conduct an initial assessment of long term care facilities whose residents test positive for CRE. The assessment is typically conducted over the phone using the “CRE in Long Term Care Facilities Initial Assessment” questionnaire.<sup>3</sup> The intent of the interview is to assess the number of residents in the facility who either have active infections or are colonized, infection control measures in place, and whether they are using or have access to the CDC CRE Toolkit. From this assessment, local health departments and/or regional epidemiologists can gauge the knowledge of the facility’s staff, and decide whether to proceed with additional interviews or site visits.

All analyses were conducted in SAS Version 9.3 and Microsoft Excel.

## RESULTS

### Organisms

From January-December 2016, 254 organisms were reported from 249 patients. Two individuals were diagnosed with 2 or more different CRE organisms. The most frequently identified organism was *Enterobacter cloacae*, with 93 (36.6%) isolates. *Enterobacter aerogenes* followed with 57 (22.4%) isolates (Table 1). The focus of the remainder of this report will be on *Enterobacter* species, *K. pneumoniae*, and *E. coli*. Any isolate not characterized to the species level is reclassified into the “Other” category as it cannot be grouped with any specific species.

Table 1. CRE Isolates 2016 West Virginia

Organism (N = 254)	N (%)
<i>Enterobacter cloacae</i>	93 (36.6)
<i>Enterobacter aerogenes</i>	57 (22.4)
<i>Klebsiella pneumoniae</i>	42 (16.5)
<i>Escherichia coli</i>	28 (11.0)
<i>Citrobacter freundii</i>	9 (3.5)
<i>Klebsiella oxytoca</i>	6 (2.4)
<i>Serratia marcescens</i>	6 (2.4)
<i>Enterobacter gergoviae</i>	2 (0.8)
<i>Raoultella ornithinolytica</i>	2 (0.8)
<i>Providencia stuartii</i>	2 (0.8)
<i>Klebsiella</i> spp.	2 (0.8)
<i>Proteus mirabilis</i>	1 (0.4)
<i>Pantoea agglomerans</i>	1 (0.4)
<i>Morganella morganii</i>	1 (0.4)
<i>Citrobacter</i> spp.	1 (0.4)
<i>Citrobacter braakii</i>	1 (0.4)

Much of the overall increase in all organisms isolated can be attributed to the change in surveillance case definition. The only exception was *Enterobacter cloacae*, which sustained a 57.8% increase in isolates from 2015, with these isolates also meeting 2015 case definition (Table 2). It is important to note that because of the change in case definition, data from 2016 is not comparable with any previous year.

<sup>2</sup> DIDE, 2016 CRE Notification Protocol <http://www.dhhr.wv.gov/oeps/disease/AtoZ/documents/cre/cre-protocol.pdf>

<sup>3</sup> DIDE, 2016 CRE LTCF Initial Assessment <http://www.dhhr.wv.gov/oeps/disease/AtoZ/Pages/CRE.aspx>

Table 2. 2016 CRE Isolates Meeting 2015 Case Definition, West Virginia

Organism	Case Definition (2015)		
	Yes	No	Total
<i>Enterobacter cloacae</i>	64 (68.8%)	29 (31.2%)	93
<i>Enterobacter aerogenes</i>	7 (12.5%)	49 (87.5%)	56
<i>Klebsiella pneumoniae</i>	36 (85.7%)	6 (14.3%)	42
Other	19 (55.9%)	15 (44.1%)	34
<i>Escherichia coli</i>	11 (39.3%)	17 (60.7%)	28
Total	137 (54.2%)	116 (45.9%)	253

Frequency Missing = 1

Urine was the most common specimen to test positive for CRE, with 202 (79.5%) (Table 3). Two-hundred and fifty-three cultures (99.6%) were clinical, and 1 (0.4%) was reported as surveillance. No cases were reported to be epidemiologically linked to other CRE cases. Review of information entered into the West Virginia Electronic Disease Surveillance System (WVEDSS) and 2016 outbreak data did not reveal any evidence of outbreak related CRE cases in 2016. Data for cases that were not marked “No” for “Outbreak Related” were either missing, or entered incorrectly.

Table 3. CRE Isolates by Surveillance Region, West Virginia, 2016; N=254

CRE Isolates by Surveillance Region, West Virginia, 2016; N = 254						
	Northwest (N=34)	Northeast (N=23)	East (N=20)	South (N=73)	West (N=43)	Central (N=61)
<b>Organism Cultured</b>						
<i>Enterobacter cloacae</i>	13 (38.2%)	6 (26.1%)	6 (30.0%)	23 (31.5%)	22 (51.2%)	23 (37.7%)
<i>Enterobacter aerogenes</i>	4 (11.8%)	9 (39.1%)	3 (15.0%)	20 (27.4%)	8 (18.6%)	13 (21.3%)
<i>Escherichia coli</i>	1 (2.9%)	2 (8.7%)	3 (15.0%)	8 (11.0%)	6 (14.0%)	8 (13.1%)
<i>Klebsiella pneumoniae</i>	10 (29.4%)	3 (13.0%)	4 (20.0%)	14 (19.2%)	3 (7.0%)	8 (13.1%)
Other	6 (17.7%)	3 (13.0%)	4 (20.0%)	8 (11.0%)	4 (9.3%)	9 (14.8%)
<b>Type of Culture</b>						
Clinical	34 (100%)	23 (100%)	19 (95.0%)	73 (100%)	42 (97.7%)	61 (100%)
<b>Specimen Source</b>						
Urine	28 (82.4%)	22 (95.7%)	13 (65.0%)	58 (79.5%)	30 (69.8%)	51 (83.6%)
Respiratory	3 (8.8%)	0	2 (10.0%)	6 (8.2%)	7 (16.3%)	5 (8.2%)
Wound	2 (5.9%)	0	2 (10.0%)	3 (4.1%)	3 (7.0%)	3 (4.9%)
Blood	0	1 (4.4%)	0	2 (2.7%)	1 (2.3%)	1 (1.6%)
Device	1 (2.9%)	0	0	1 (1.4%)	0	0
Other	0	0	3 (15.0%)	2 (2.7%)	2 (4.7%)	1 (1.6%)
Missing	0	0	0	1 (1.4%)	0	0
<b>Outbreak Related*</b>						
No	34 (100%)	21 (91.3%)	20 (100%)	68 (93.2%)	42 (97.7%)	60 (98.4%)
<b>Epi Linked to other CRE*</b>						
No	33 (97.1%)	21 (91.3%)	19 (95.0%)	67 (91.8%)	42 (97.7%)	58 (95.1%)

\*Percent < 100 indicates missing or incomplete data

## Demographics

The mean age of cases in 2016 was 65.0 years, with a range of 10 months to 98 years. One hundred and seventy-seven (77.1%) were female. The majority of cases were white, with 173 (69.5%). One hundred and seventy-five (70.3%) were identified as not Hispanic or Latino, and for 72 (28.9%), information about ethnicity was missing.

The highest number of cases resided in Kanawha County with 38 (15.3%), followed by Raleigh County residents with 19 (7.6%). When analyzed by surveillance region, the Southern region reported 70 (28.1%) cases, followed by the Central region with 60 (24.1%). Figure 3 shows the distribution of CRE cases by surveillance region.

Seventy (28.1%) cases were hospitalized at the time of specimen collection, and twenty (8.0%) died. Seven (35.0%) deaths occurred in the Central surveillance region and 6 (30.0%) occurred in the Western surveillance region. Of the 46 (18.5%) cases who resided in long term care facilities, assessments were performed for 33 (71.7%). An assessment was not performed for 10 (21.7%) cases, and 3 (6.5%) results were missing.

Table 4. CRE Cases by Demographic Variable and Surveillance Region, West Virginia, 2016; N=249

CRE Cases by Demographic Variable and Surveillance Region, West Virginia, 2016; N=249						
	Northwest (N=34)	Northeast (N=22)	East (N=20)	South (N=70)	West (N=43)	Central (N=60)
<b>Age, years (Avg. or N (%))</b>	66.6	64.8	56.2	64.5	65.4	67.4
0-4	0	0	<5	0	<5	0
5-24	<5	<5	<5	<5	0	<5
25-44	<5	<5	<5	9 (12.9%)	<5	<5
45-64	9 (26.5%)	5 (22.7%)	<5	22 (31.4%)	18 (41.9%)	17 (28.3%)
≥65	21 (61.8)	14 (63.6%)	11 (55.0%)	38 (54.3%)	21 (48.9%)	37 (61.7%)
<b>Sex</b>						
Female	5 (56.0%)	7 (100.0%)	7 (64.0%)	25 (66.1%)	8 (67.1%)	12 (55.0%)
<b>Race</b>						
White	7 (78.0%)	6 (86.0%)*	9 (82.0%)*	31 (82.1%)*	12 (100.0%)	18 (82.0%)*
<b>LTCF Resident</b>						
Yes	<5	<5	<5	18 (47.4%)	0*	7 (32.0%)
<b>Hospitalized</b>						
Yes	<5	<5	<5	15 (39.5%)*	6 (50.0%)	8 (36.3%)*
* indicates Missing or Unknown data						

CRE incidence rates for the 6 surveillance regions were calculated per 100,000 population using 2010 Census data. Statewide, the rate of new CRE cases identified was 16.9 per 100,000 persons. The Southern region of the state saw the highest incidence with 22.7 new CRE cases per 100,000 persons (Table 5).

Table 5. CRE Incidence by Surveillance Region, West Virginia, 2016

CRE Incidence by Surveillance Region, West Virginia, 2016			
	Population (2010 Census)	Cases (No. of Organisms)	Incidence (per 100,000 population)
<b>Southern</b>	322,213	73	22.7
<b>Central</b>	312,852	61	19.5
<b>Western</b>	313,985	43	13.7
<b>Northwestern</b>	309,445	34	11.0
<b>Northeastern</b>	296,912	23	7.7
<b>Eastern</b>	297,587	20	6.7
<b>State Total</b>	1,540,142	254	16.9

Incidence was also calculated for each county, and is shown per 10,000 population to more accurately reflect the average population size of West Virginia counties. Figure 2 shows CRE case counts by county.

Figure 1. CRE Incidence per 10,000 Population by County, West Virginia, 2016; N=254

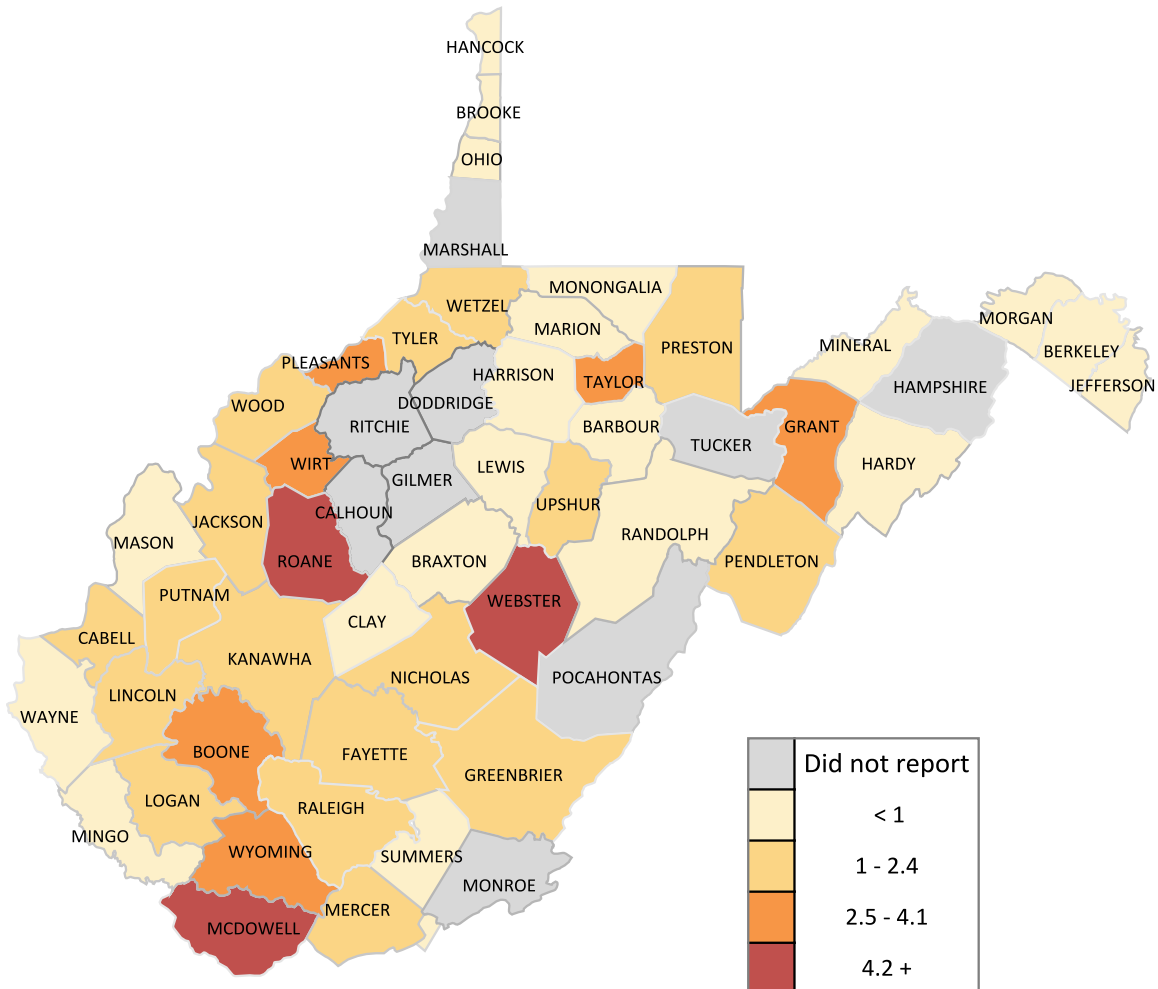
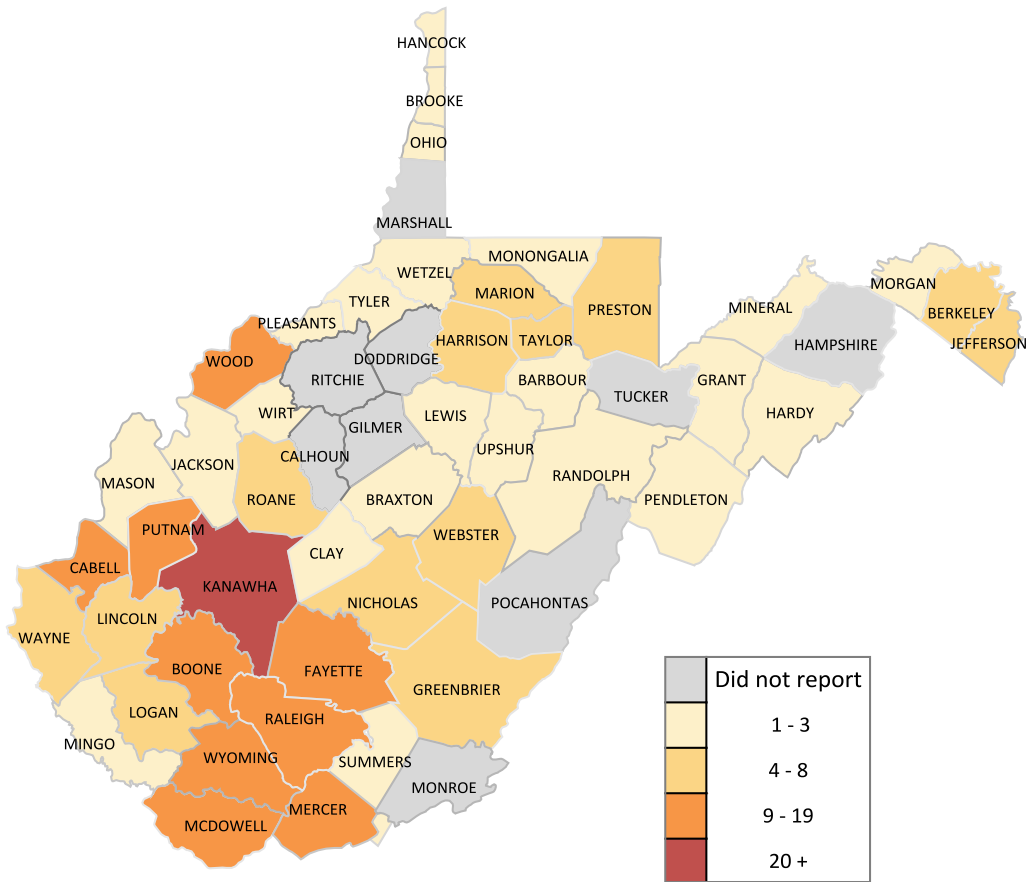


Figure 2. CRE Case Counts by County, West Virginia, 2016; N=254



## DISCUSSION

The spread of carbapenem resistance among Enterobacteriaceae is considered an urgent public health threat by the CDC. The data presented in this report paint a concerning picture of CRE’s foothold on West Virginia. A large portion of the burden rests within the State’s southern counties; however, health facilities throughout the State should implement the CDC CRE prevention and control plan as no health facility is likely to remain unaffected.

The change in the 2016 case definition is responsible for much of the increase seen in CRE organisms across the state. After reclassifying 2016 cases according to the less broad 2015 definition, case counts remained mostly stable and a decrease was seen for some organisms such as *Enterobacter aerogenes* and *Klebsiella pneumoniae*. *Enterobacter cloacae* case counts remained high, and demonstrated a 57.8% increase in cases after accounting for the change in definition. This represents a shift in the dominant organism in West Virginia, which has historically been *Klebsiella pneumoniae*. In addition, 73.1% of all *Enterobacter cloacae* isolates, regardless of reclassification, were found in patients who denied any stays in long term care facilities. A recent study conducted by the Veterans Administration (VA) suggested a

“second epidemic” of CRE is emerging, with *Enterobacter cloacae* at the helm.<sup>4</sup> Gomez-Simmonds et al. also noted *Enterobacter cloacae*’s increasing incidence, as well as its ability to adapt and gain new resistance mechanisms with relative ease.<sup>5</sup> Innate characteristics of the organism may account for some of its expansion across the State, but additional studies will need to be conducted in order to truly assess the potential reasons for the substantial increase in *Enterobacter cloacae* isolates. The implementation of resistance mechanism testing at DHHR’s West Virginia Office of Laboratory Services (OLS) may begin to shed light on the issue. Incorporating additional exposure variables into the CRE case investigation process, such as an assessment of home health service utilization, may also reveal undiscovered transmission avenues.

These data should be interpreted with some caution. West Virginia conducts passive surveillance of CRE and relies on laboratory or facility reporting of cases. Although CRE is a reportable condition for laboratories in West Virginia, some cases may go unreported. Determining the true cause for hospitalization is not possible during the analysis of these data as the information gathered pertains only to patient status at the time of specimen collection. True cause of death is similarly unclear.

There are some limitations to determining an accurate CRE incidence, chief among them assessing the population actually at risk. While some CRE infections may be acquired in the community, the majority have historically been associated with exposure to health care facilities and prolonged use of broad spectrum antibiotics. Hospital populations are not stable, making it difficult to ascertain who is most at risk. Though somewhat more stable, nursing home populations change over the course of a year as well. The number of people residing in nursing homes is also relatively small, despite a generally older population in West Virginia. According to the Kaiser Family Foundation,<sup>6</sup> the population residing in West Virginia certified nursing facilities was 8,852 in 2014—a mere 0.5% of the estimated total state population in 2014. As the rates for this report were calculated using the West Virginia population as a whole, the results should be interpreted with some caution, and may be much higher than stated here. Additional studies would need to be conducted to accurately discern the most important risk factors for developing an infection with a carbapenem resistant organism in West Virginia.

West Virginia does not currently track which laboratories perform resistance mechanism testing, such as modified Hodge testing, to detect carbapenemase production among CRE isolates. This type of testing is not necessary to direct clinical care of patients, but it is useful in planning aggressive infection prevention efforts in areas with a high prevalence of carbapenemase producing CRE organisms (CP-CRE). Carbapenemases, enzymes that inactivate carbapenem and many other classes of antibiotics, are typically located on mobile bits of genetic material called plasmids. These plasmids are easily exchanged between different bacteria, thus facilitating rapid spread of carbapenem resistance. The CDC recommends more stringent infection prevention practices in areas where CP-CRE are prevalent as these organisms are suspected to be responsible for much of the spread throughout the country.<sup>7</sup>

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<sup>4</sup> Wilson, B. M., El Chakhtoura, N. G., Patel, S., Saade, E., Donskey, C. J., Bonomo, R. A....Perez, F. (2017). Carbapenem-Resistant *Enterobacter cloacae* in Patients from the US Veterans Health Administration, 2006–2015. *Emerging Infectious Diseases*, 23(5), 878-880. <https://dx.doi.org/10.3201/eid2305.162034>.

<sup>5</sup> Gomez-Simmonds, A., et al. (2016) Evidence from a New York City hospital of rising incidence of genetically diverse carbapenem-resistant *Enterobacter cloacae* and dominance of ST171, 2007-14. *J Antimicrob Chemother* 2016, doi:10.1093/jac/dkw132.

<sup>6</sup> Kaiser Family Foundation, 2016 Total Number of Residents in Certified Nursing Facilities. <http://kff.org/>

<sup>7</sup> CDC, Healthcare-associated Infections (HAIs)-FAQs about Choosing and Implementing a CRE Definition



Despite the limitations, these data have implications for important infection prevention activities. Health care facilities of all types in all regions of the state should adhere to recommendations for standard and contact precautions for patients who are either infected or colonized with any multi drug resistant organism (MDRO), and especially CRE organisms. Special attention must be paid to hand hygiene practices and personal protective equipment (PPE) usage among health care facility staff, and facilities should be conducting regular audits of personnel hand hygiene and PPE compliance. Tools to facilitate the implementation of these audits are available from DHHR's Division of Infectious Disease Epidemiology (DIDE). A robust infection prevention program also includes antibiotic stewardship implemented facility wide. These programs should include appropriate use guidelines for first line treatments of common conditions that are supported by evidence based practices. Educating providers, patients, and the general public on the dangers of overusing antibiotics remains an important investment of time and effort on the part of state and local health departments.