



State of Utah

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Utah Department of Health

Joseph K. Miner, MD, MSPH, SACPM, FACPM
Executive Director

Disease Control and Prevention

Heather Borski, MPH, MCHES
Division Director

Bureau of Epidemiology

Melissa Dimond, MPH
Bureau Director

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Re: Laboratory guidance for reporting and isolate submission of antibiotic resistant organisms to the Utah Department of Health and updates to the Utah Communicable Disease Rule

Dear Laboratory Managers, Microbiology Supervisors and Infection Preventionists,

Thank you for your assistance during the past few years to raise awareness of antibiotic resistance in Utah. In 2017, laboratories reported 148 cases of carbapenem resistant *Enterobacteriaceae* (CRE) and carbapenem resistant *Acinetobacter* (CRA) to the Utah Department of Health (UDOH). Eight of the reported isolates tested positive for a carbapenemase gene; four with KPC genes, two with NDM genes, one with the OXA-48 gene and one with a positive phenotypic test. This data probably under represents Utah's actual multi-drug resistant organism (MDRO) disease burden. Your continued efforts regarding reporting and submission of isolates to public health will increase knowledge regarding Utah's current burden of these concerning antibiotic resistant organisms and help facilitate future prevention activities in Utah's healthcare facilities and communities. Several reporting issues and needs are further explained in this letter.

Additions to Utah reportable conditions and isolate submission

Updates to Utah's Communicable Disease Rule (R386-702) will aid increased understanding of Utah's MDRO burden. We respectfully request that laboratory staff and infection preventionists be aware of these updates. Utah's Communicable Disease Rule requires laboratories to submit isolates of all carbapenem-resistant *E.coli*, carbapenem-resistant *Enterobacter* species, carbapenem-resistant *Klebsiella* species, carbapenem-resistant *Acinetobacter* species, carbapenem-resistant *Pseudomonas aeruginosa* isolates, and any isolates of *Candida auris* and *Candida haemulonii* to the Utah Public Health Laboratory (UPHL) for further characterization. Further study of these isolates can provide valuable genetic information for cluster identification and outbreak investigation. The UDOH fax number for reporting is 801-538-9923.

A list of current reporting requirements with specific disease and reporting timelines will soon be updated and available at http://health.utah.gov/epi/reporting/Rpt_Disease_List.pdf. Until this link is updated, current changes effective as of January 2, 2018 are available through the Administrative Rules Bulletin from November 15, 2017 at https://rules.utah.gov/publicat/bull_pdf/2017/b20171115.pdf. Specific reporting expectations are outlined in the following table, with new expectations highlighted in yellow.

Table I. Surveillance for Multidrug Resistant Organisms in Utah, 2018

Genus & species	Antibiotic Susceptibility Criteria	Submitters
<p><i>E. coli</i></p> <p><i>Klebsiella</i> spp.</p> <p><i>Enterobacter</i> spp.</p> <p>CRE</p>	<p>Resistant to ≥ 1 carbapenem: MIC ≥ 4 $\mu\text{g/ml}$ for meropenem, imipenem, and doripenem OR MIC ≥ 2 $\mu\text{g/ml}$ for ertapenem OR K-B zone* ≤ 19 mm for meropenem, imipenem, and doripenem OR K-B zone ≤ 18 mm for ertapenem</p>	<p>Statewide reporting and submission of both screening/surveillance and clinical isolates</p> <p>(*Please Note: there is no current requirement for reporting/submission of other members of the <i>Enterobacteriaceae</i> family not listed)</p>
<p><i>Acinetobacter</i> spp.</p> <p>CRA</p>	<p>Resistant to ≥ 1 carbapenem: MIC ≥ 8 $\mu\text{g/mL}$ for meropenem, imipenem, and doripenem OR K-B zone ≤ 14 mm for doripenem and meropenem OR K-B zone ≤ 18 mm for imipenem</p>	<p>Statewide reporting and submission</p>
<p><i>Pseudomonas aeruginosa</i></p> <p>CRPA</p>	<p>Resistant to ≥ 1 carbapenem: MIC ≥ 8 $\mu\text{g/mL}$ for any carbapenem OR K-B zone ≤ 15 mm for any carbapenem</p>	<p>Statewide reporting by Electronic Lab Reporting (ELR) for surveillance only and submission</p>
<p><i>Candida auris</i></p>	<p>None</p>	<p>Statewide reporting and submission of both screening/surveillance clinical isolates</p>
<p><i>Candida haemulonii</i></p> <p><i>Other rare Candida spp. or Candida spp. from sterile sites implicated in invasive disease that cannot be accurately speciated**</i></p>	<p>None</p>	<p>Statewide reporting and submission of both screening/surveillance clinical isolates</p>
<p>Vancomycin-resistant <i>Staph aureus</i> (VRSA)*</p>	<p>Resistant to vancomycin: MIC ≥ 16 $\mu\text{g/mL}$ K-B zone should not be used to determine resistance to vancomycin</p>	<p>Statewide within 24 hrs (immediately notifiable)</p>
<p>Methicillin-susceptible <i>Staph aureus</i> (MSSA) and Methicillin- resistant <i>Staph aureus</i> (MRSA) from sterile body sites</p>	<p>(MSSA) Oxacillin MIC ≤ 2 $\mu\text{g/ml}$ Cefoxitin MIC ≤ 4 $\mu\text{g/ml}$ K-B zone $\geq 22\text{mm}$ for Cefoxitin (MRSA) Resistant to Oxacillin: MIC ≥ 4 $\mu\text{g/mL}$ K-B zone ≤ 21 mm for Cefoxitin</p>	<p>Statewide reporting by ELR</p>

*Vancomycin-intermediate *Staph aureus* (VISA) was previously reportable but has been removed and is no longer reportable, but suspected VISA isolates should be verified through repeat-testing to confirm it is not VRSA (MIC \geq 16 μ g/mL)

**Exclude *C. albicans*, *C. parapsilosis*, *C. dubliniensis*, *C. lusitaniae*, *C. tropicalis*, and *C. krusei* and any other yeast infections that do not fit the above criteria.

Reporting of antibiotic susceptibility testing (AST) results and breakpoints

Full panel antibiotic susceptibility test results including minimum inhibitory concentration (MIC) values or Kirby Bauer (K-B) zone sizes, and results suppressed to the ordering clinician, are reportable (R386-702-6, R386-702-7). Reports should include interpretations, complete antibiotic susceptibilities after repeat testing and standard purity checks, and suppressed results to ensure accurate, complete, and standardized reporting. For more information regarding this reporting requirement, please refer to the Council of State and Territorial Epidemiologists (CSTE) 2017 Position Statement 17-ID-04, and the *Recommendation: Use the most current Clinical & Laboratory Standards Institute (CLSI) guidelines (M100-S27) for minimum inhibitory concentration (MIC) breakpoints*, available at http://em100.edaptivedocs.info/Login.aspx?_ga=2.127404686.2066098109.1514932533-945308666.1514932533 (free web version).

Reporting of additional carbapenemase testing (CP)

In addition to antibiotic susceptibilities, laboratories are required to report whether any phenotypic testing for CRE (e.g. mCIM test), or PCR testing of carbapenemase-producing genes for CRE or CRA, was performed on the isolate by the primary testing facility. This reporting will avoid duplication and assist further investigation needs. This requirement has been added to in R386-702-6 and R386-702-7.

All individual carbapenemase test results (positive, negative, equivocal, indeterminate), including the method used, are reportable when performed on the following organisms: (i) Resistant to a carbapenem, or with demonstrated carbapenemase, in: (A) Acinetobacter species, (B) Enterobacter species, (C) Escherichia coli, and (D) Klebsiella species."

Laboratory saving, storing, and submission of suspected MDRO isolates

Laboratories are requested to save all suspected MDRO isolates and submit them to the Utah Public Health Laboratory (UPHL) as quickly as possible for confirmation and further testing. If deemed necessary, UPHL will forward isolates to the Antibiotic Resistance Laboratory Network (ARLN) laboratory in Texas or the Centers for Disease Control and Prevention (CDC) laboratory as appropriate. Please note, submission of clinical material does not replace the requirement for laboratories to report the event to public health (see R386-702-6, R386-702-7).

UPHL has the testing capability to identify the five major classes of carbapenemase gene families (KPC, NDM, VIM, IMP-1 and OXA-48) by PCR. However, carbapenemase gene testing is reserved for CRA resistant to all first line antibiotics, and for CRE and CRPA following a positive phenotypic test. UPHL will send carbapenem-producing (CP) CRE isolates that test negative for the aforementioned genes to the Texas ARLN lab to test for potential novel carbapenemase mechanisms. The public health isolate submission form can be found at: <http://health.utah.gov/lab/infectious-diseases/documents/UPHL%20ID%20requisition%20form.pdf>.

Reporting of all clinical and screening/surveillance isolates to public health

Carbapenem-resistant cultures often result from diagnostic studies for bacteremia, pneumonia, urinary tract infection, wounds, or abscesses, or as asymptomatic colonization. Mounting evidence suggests a long-term patient reservoir in patients exposed to long-term care facilities (Bhargava et al, 2014). All identified CRE, CRA, and CRPA results are reportable in Utah, including results from identified colonized patients, regardless of infection status. The Utah Communicable Disease Rule requires reporting of each case and isolate submission to UPHL, even if the patient is known to have had a previously reported CRE or CRA isolate.

Candida auris/haemulonii and other Candida spp.

Reporting of *Candida auris* and *Candida haemulonii* are included in the updated Communicable Disease Rule as these two, closely-related, emerging multi-drug resistant yeast strains have been found in invasive infections in healthcare settings, and are often associated with high mortality rates. Although several cases of *C. auris* have been reported in the United States, no cases have been reported in Utah to-date (CDC, 2017). Future surveillance will provide better understanding regarding transmission, resistance patterns, and treatment response of *C. auris* and *C. haemulonii* (CSTE, 2017 17-ID-03, p.2).

Although most laboratories can broadly classify yeast, most laboratories have limited capabilities to speciate and perform susceptibility testing on yeast isolates. To this end, many laboratories have protocols for submitting yeast isolates to reference laboratories from sterile sites, and from persistent or difficult to treat infections. Furthermore, because *C. auris* can often be misidentified as other yeast (especially *C. haemulonii*), and requires specialized identification methods (CSTE, 2017 Position Statement 17-ID-03), additional confirmatory testing is necessary to rule out *C. auris*. Please note the following CSTE position statement:

“Unlike C. auris, strains of C. haemulonii are typically unable to grow above 37C; therefore, C. auris should be suspected when C. haemulonii is identified on culture of invasive body sites (e.g., blood) unless the method used can reliably detect C. auris” (CSTE, 2017 Position Statement 17-ID-03)).

Consequently, Utah’s Communicable Disease Rule requires mandatory reporting and submission of all *C. auris*, confirmed and suspected, and *C. haemulonii* isolates to UPHL for referral to the Texas ARLN Lab for identification and typing. Correct identification and reporting of *C. auris* is essential for appropriate containment efforts. The following tables outline appropriate diagnostic methods and laboratory reporting protocols for *C. auris*:

Table II. Currently approved *Candida auris* methods of identification* (CDC, 2017)

Methods currently approved for <i>C. auris</i> identification	Methods NOT currently approved to identify <i>C. auris</i>
<ul style="list-style-type: none">• Whole genome sequencing or marker gene sequencing of the internal transcribed spacer and D1/D2 regions• Bruker’s 6903 MSP RUO databases for Biotyper• Specific bioMérieux identification platforms:<ul style="list-style-type: none">- VITEK 2 YST (with Ver 8.01 software)- VITEK (MALDI-TOF) MS RUO (with Saramis Ver 4.14 database and Saccharomycetaceae update)	<ul style="list-style-type: none">• API 20C AUX (bioMérieux, Marcy l’Etoile, France)• BD Phoenix (BD Diagnostics, Sparks, MD)• MicroScan (Beckman Coulter, Pasadena, CA)

*Methods are continuously evolving and advancing. This list is up to date as of February 16, 2017. CDC's MicrobeNet (<https://www.cdc.gov/microbenet/index.html>) is a tool that provides information for the most relevant laboratory identification methods, including MALDI-TOF, which has been curated by subject matter experts. The Biotyper Classification Module, recently released as a collaboration between CDC and Bruker, provides MicrobeNet users with access to Bruker's most up-to-date database and CDC spectral libraries. The strains of *C. auris* represented in the MicrobeNet database have been proven to accurately classify to the species level on the Biotyper. (Source: CSTE 17-ID-03)

Table III. Utah *Candida auris* and *Candida haemulonii* public health reporting criteria

Criterion		
<i>Clinical Evidence</i>		
Health care record diagnosis of <i>Candida auris</i>	S	
Health care record diagnosis of <i>Candida haemulonii</i>	S	
Death certificate lists as cause of death or significant condition contributing to death: <i>C. auris</i>	S	
Death certificate lists as cause of death or significant condition contributing to death: <i>C. haemulonii</i>	S	
<i>Laboratory Evidence</i>		
<i>C. auris</i> identified on culture by a diagnostic instrument equipped to identify it (e.g., MALDI-TOF or some phenotypic methods)		S
<i>C. haemulonii</i> identified by a laboratory instrument not equipped to detect <i>C. auris</i> (as of February 2017, any method other than MALDI-TOF or ribosomal DNA sequencing)		S
<i>Rhodotorula glutinis</i> identified by API 20C, and the characteristic red color of <i>R. glutinis</i> is not present		S
<i>Candida sake</i> identified by API 20C		S
<i>Candida catenulata</i> identified by BD Phoenix		S
<i>Candida catenulata</i> , <i>Candida famata</i> , <i>Candida guilliermondii</i> , or <i>Candida lusitanae</i> identified by MicroScan		S
<i>Candida</i> spp. (if unable to further speciate after validated method of <i>Candida</i> identification attempted)		S

S = This criterion alone is sufficient to report a case. A requisition or order for any of the "S" laboratory tests is sufficient to meet the reporting criteria. (Source: CSTE 17-ID-03)

UDOH and UPHL contact information regarding MDRO reporting requirements

For any questions regarding MDRO reporting requirements as specified by the Utah Communicable Disease Rule, or for assistance with investigation questions or needs, please contact the UDOH MDRO Epidemiologists, Maureen Vowles (mvowles@utah.gov, (801) 538-6172) or Amanda Smith (amandarsmith@utah.gov, (801) 538-6247). For questions regarding submission, testing, courier support, shipping requirements, or further information regarding available testing, please contact Lori Smith, Bacteriology Supervisor, (lhsmith@utah.gov, (801) 965-2503) or Alessandro Rossi, Infectious Diseases Chief Scientist, (arossi@utah.gov, (801) 965-2554) at the UPHL.

The UDOH is grateful for your continued commitment to quality laboratory practices and patient care, and for your cooperation in ensuring reporting and isolate submission are consistent with requirements of Utah's Communicable Disease Rule. Together, we can prevent transmission and enhance containment of these concerning MDROs in Utah.

Sincerely,



Karen Singson, RN, MSN, CIC
HAI/AR Program Manager



Melissa Dimond, MPH
Director, Bureau of Epidemiology



Robyn Atkinson-Dunn, PhD, HCLD/PHLD
Director, Utah Public Health Laboratory



Angela C. Dunn, MD, MPH
State Epidemiologist

References

Bhargava, A., Hayakawa, K., Silverman, E., Halder, S., Alluri, K., Datla, S., Divit, S., Kuchipudi, V., Mappavarapu, K., Lephart, P., Marchaim, D., and Kaye, K. (2014) 'Risk factors for colonization due to carbapenem-resistant Enterobacteriaceae among patients exposed to long-term acute care and acute care facilities.' *Infection Control Hospital Epidemiology*, Vol. 35, Issue No. 4, pp.398-405. [Online] Available from: <https://www.ncbi.nlm.nih.gov/pubmed/24602945>

Centers for Disease Control and Prevention. – *Candida auris* Clinical Update – September 2017. [Online] Available from: <https://www.cdc.gov/fungal/diseases/candidiasis/c-auris-alert-09-17.html>

Council of State and Territorial Epidemiologists CSTE (2017) Position statements can be found as follows:

17-ID-04. Public Health Reporting and National Notification of Carbapenemase Producing Carbapenem-Resistant *Enterobacteriaceae* (CP-CRE) for *E. coli*, *Klebsiella* spp. And *Enterobacter* spp. [Online] Available from:

https://www.cste2.org/Publications/CP_CRE_Operational_guidance_20170601.pdf

17-ID-03 Standardized Case Definition for *Candida auris* causing clinical infection and colonization in people. [Online] Available from:

<http://c.ymedn.com/sites/www.cste.org/resource/resmgr/2017PS/2017PSFinal/17-ID-03.pdf>

CC: Utah Local Health Departments' Healthcare Associated Infections Epidemiologists