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TO: Clinical and Public Health Laboratories, Hospitals, Local Health Departments

FROM: New York State Department of Health Health (NYSDOH)
Wadsworth Center and Division of Epidemiology

HEALTH ADVISORY:

ANTIFUNGAL-RESISTANT CANDIDA AURIS AND SUSCEPTIBILITY TESTING OF NEW INVESTIGATIONAL DRUGS / DRUG-COMBINATIONS

Please distribute immediately to:

Laboratory Directors, Infection Preventionists, Medical Directors, Administrators, Hospital Epidemiologists, Directors of Environmental Services, Infectious Disease Physicians, Critical Care Medicine Physicians, and Risk Managers

Purpose:

The clinical and public health community is on high alert, because of the alarming rise in the incidence and spread of drug-resistant *Candida auris* in New York since 2016. Recent reports describe multidrug-resistant and panresistant *C. auris* isolates from New York. This advisory describes a new New York State Department of Health-Wadsworth Center (NYSDOH-WC) laboratory service for testing of novel investigational drugs (Ibrexafungerp® and Manogepix®) and two-antifungal drug combination testing with flucytosine. These laboratory services aim to provide healthcare professionals and public health experts with additional tools to manage drug-resistant *C. auris*.

Background:

Candida auris has been shown to be responsible for severe illnesses among hospitalized patients in the New York metropolitan area. Of 1,208 confirmed *C. auris* clinical cases tracked by the CDC, 717 (approximately 60%) were reported from New York and New Jersey. The New York *C. auris* cases are concentrated among hospitalized patients and nursing home residents, with 581 clinical cases and 785 screening cases confirmed as of August 21, 2020. An earlier analysis of New York *C. auris* cases indicated 23 (45%) of the 51 clinical case-patients died within 90 days. The New York State Department of Health (NYSDOH) laboratory scientists and epidemiologists conducted unprecedented surveillance and testing for *C. auris*. To date, over 20,000 clinical samples from 194 facilities were processed in the NYSDOH laboratory. The CLSI broth microdilution

method (BMD) was used for antifungal susceptibility testing of nearly 1,100 *C. auris* isolates. The results were interpreted according to CDC guidelines in the absence of susceptibility breakpoints for *C. auris*. *Candida auris* isolates in New York metropolitan area are resistant to fluconazole and many strains also showed elevated MICs to voriconazole, amphotericin B, flucytosine, and echinocandins. More recently, pan-resistant *C. auris* isolates (resistant to two or more azoles, amphotericin B, and echinocandins) were recorded in New York. Clinicians and public health professionals face challenges in dealing with the large, sustained outbreak of *C. auris* in New York that is exacerbated by the reported pattern of antifungal resistance.

A conceptual framework supports using drug combinations to combat the threat of antimicrobial resistance. Therefore, NYSDOH-WC scientists investigated the efficacy of two-drug combinations against drug-resistant *C. auris* strains. An earlier published test method, standardized by several multi-laboratory studies, was used for the testing of amphotericin B-flucytosine, anidulafungin-flucytosine, caspofungin-flucytosine or micafungin-flucytosine. The findings suggested that *C. auris* strains with various resistance patterns were susceptible to low dose combinations of an existing drug and flucytosine. The results were later confirmed with a time-kill assay. Two new investigational drugs being developed for *Candida* infections (Ibrexafungerp® and Manogepix®) were tested using BMD against NY *C. auris* isolates in collaboration with the respective manufacturers. Ibrexafungerp® demonstrated low MICs against *C. auris*, including panresistant isolates relative to comparator drugs. Manogepix® demonstrated lower MICs than ten comparator drugs against *C. auris* isolates, and this activity was independent of the clinical, environmental or surveillance source of *C. auris*. Pursuant of these developments, NYSDOH-WC is offering laboratory service for the testing of new investigational drugs (Ibrexafungerp® and Manogepix®) and two-antifungal drug combination testing with flucytosine.

Implementation of the Wadsworth Center antifungal combination testing or susceptibility testing for new investigational drugs:

To submit isolates for Wadsworth Center antifungal combination testing with flucytosine/ new investigational drug susceptibility testing, the following needs to be submitted to Wadsworth Center Mycology Laboratory:

- *Candida auris* isolate from blood, sterile body site or body fluid
- Prior antifungal susceptibility test results for single drugs
- Brief justification for the antifungal combination with flucytosine/new investigational drug testing (Ibrexafungerp® and Manogepix®)

Please be advised the antifungal susceptibility test results will be available within 3-5 working days. NYSDOH-WC staff are available to assist with the test interpretation and other relevant details. Please contact mycology@health.ny.gov with any questions.