4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2017-N-5925]

21st Century Cures Act: Annual Compilation of Notices of Updates from the Susceptibility Test Interpretive Criteria Web Page, 2021 and 2022 Updates; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is announcing the availability of the Agency's annual compilation of notices of updates to the Agency's Susceptibility Test Interpretive Criteria web page with updates made in 2021 and 2022. The Agency established the Susceptibility Test Interpretive Criteria web page on December 13, 2017, and since establishment has provided updates to both the format of the web pages and to the susceptibility test interpretive criteria identified and recognized by FDA on the web pages. FDA is publishing this notice in accordance with procedures established by the 21st Century Cures Act (Cures Act).

DATES: This notice is published in the *Federal Register* on [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: You may submit either electronic or written comments and information as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: https://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to https://www.regulations.gov will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment

does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2017-N-5925 for "Susceptibility Test Interpretive Criteria Recognized and Listed on the Susceptibility Test Interpretive Web Page; Request for Comments." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at https://www.regulations.gov or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information

you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on https://www.regulations.gov. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to https://www.regulations.gov and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

FOR FURTHER INFORMATION CONTACT: Deborah (Wang) Kim, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 6349, Silver Spring, MD 20993-0002, 301-796-9053, Deborah.Wang@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

Section 511A of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 360a-2), as added by section 3044 of the Cures Act (Pub. L. 114-255), was signed into law on December 13, 2016. This provision clarified FDA's authority to identify and efficiently update

susceptibility test interpretive criteria, including through the recognition by FDA of standards established by standards development organizations (SDOs). It also clarified that sponsors of antimicrobial susceptibility testing devices may rely upon listed susceptibility test interpretive criteria to support premarket authorization of their devices, provided they meet certain conditions, which allows for a more streamlined process for incorporating up-to-date information into such devices.

In the *Federal Register* notice of December 13, 2017 (82 FR 58617), FDA announced the establishment of the Susceptibility Test Interpretive Criteria web page. This web page recognizes susceptibility test interpretive criteria established by an SDO that fulfills the requirements under section 511A(b)(2)(A) of the FD&C Act; identifies when FDA does not recognize, in whole or in part, susceptibility test interpretive criteria established by an SDO; and lists susceptibility test interpretive criteria identified by FDA outside the SDO process. The susceptibility test interpretive criteria listed by FDA on the Susceptibility Test Interpretive Criteria web page is deemed to be recognized as a standard under section 514(c)(1) of the FD&C Act (21 U.S.C. 360d(c)(1)). The Susceptibility Test Interpretive Criteria web page can be found at https://www.fda.gov/STIC.

On March 1, 2018, FDA published a notice in the *Federal Register* (83 FR 8883) requesting comments on FDA's initial susceptibility test interpretive criteria recognition and listing determinations on the Susceptibility Test Interpretive Criteria web page (https://www.federalregister.gov/documents/2018/03/01/2018-04175/susceptibility-test-interpretive-criteria-recognized-and-listed-on-the-susceptibility-test). FDA may consider information provided by interested third parties as a basis for evaluating new or updated interpretive criteria standards (section 511A(c)(2)(B) of the FD&C Act); third parties should submit any information they wish to convey to the Agency to Docket No. FDA-2017-N-5925. If comments are received, FDA will review those comments and will make, as appropriate, updates to the recognized standards or susceptibility test interpretive criteria.

At least every 6 months after the establishment of the Susceptibility Test Interpretive Criteria web page, FDA is required, as appropriate to: (1) publish on that web page a notice recognizing new or updated susceptibility test interpretive criteria standards, or recognizing or declining to recognize parts of standards; (2) withdraw recognition of susceptibility test interpretive criteria standards, or parts of standards; and (3) make any other necessary updates to the lists published on the Susceptibility Test Interpretive Criteria web page (section 511A(c)(1)(A) of the FD&C Act). FDA has provided notices of updates on the Susceptibility Test Interpretive Criteria web page, which can be found here: https://www.fda.gov/drugs/development-resources/notice-updates. Interested parties may also sign up to receive emails informing them of these updates as they occur by using the link provided either on the main Susceptibility Test Interpretive Criteria web page (https://www.fda.gov/STIC) or on the updates page.

Once a year, FDA is required to compile the new notices published on the Susceptibility Test Interpretive Criteria web page, publish them in the *Federal Register,* and provide for public comment (see section 511A(c)(3) of the FD&C Act). This *Federal Register* notice satisfies that requirement. If comments are received, FDA will review them and make updates to the recognized standards or susceptibility test interpretive criteria as needed.

II. Annual Compilation of Notices, 2021: Web Page

Table 1.--Notices of Updates to Recognized or Updated Susceptibility Test Interpretive Criteria by Drug[1]

Drug	Route of Administration	Action Taken	Therapeutic Category	Date
Azithromycin	Oral, Injection	For *Neisseria gonorrhoeae*, FDA has reviewed susceptibility test interpretive criteria and concludes no changes are needed at this time. (Rationale available at https://www.fda.gov/drugs/development-resources/rationale-fdas-position-azithromycin-susceptible-only-breakpoint-neisseria-gonorrhoeae.)	Antibacterial	10/14/21
Cefazolin	Injection	For Enterobacterales, FDA has reviewed susceptibility test interpretive criteria and the updated standard is recognized. (Rationale available at https://www.fda.gov/drugs/development-resources/rationale-fdas-position-cefazolin-breakpoints-enterobacterales.)	Antibacterial	10/14/21

Drug	Route of Administration	Action Taken	Therapeutic Category	Date
Cefiderocol	Injection	FDA recognizes M100 MIC standard for *Enterobacteriaceae.*	Antibacterial	10/14/21
Ceftolozane; tazobactam	Injection	FDA recognizes M100 standard for *Haemophilus influenzae.*	Antibacterial	10/14/21
Colistimethate	Injection	FDA does not recognize M100 standard for *Enterobacteriaceae.*	Antibacterial	10/14/21
Imipenem/cilastatin/ relebactam	Injection	FDA recognizes M100 standard for *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and anaerobes.	Antibacterial	10/14/21
Lefamulin	Oral, Injection	FDA recognizes M100 standard for *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Haemophilus influenzae.*	Antibacterial	10/14/21
Polymyxin B	Injection	FDA does not recognize M100 standard for *Enterobacteriaceae* and *Pseudomonas aeruginosa*.	Antibacterial	10/14/21
Telithromycin	Oral	FDA has removed telithromycin susceptibility test interpretive criteria as the drug is no longer approved in any application under section 505 of the FD&C Act (21 U.S.C. 355)(see 84 FR 47309).	Antibacterial	10/14/21

[1] M100 standard in the table refers to Clinical and Laboratory Standards Institute (CLSI) Performance Standards for Antimicrobial Susceptibility Testing, 31st ed. CLSI supplement M100; 2021.

III. Annual Compilation of Notices, 2022: Susceptibility Test Interpretive Criteria Web Page

A. Updates to Standards Recognition

As of May 18, 2022, the following standards are no longer recognized: "Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing. 31st ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2021."

As of May 18, 2022, with certain exceptions, FDA recognizes the standards published in: "Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing. 32nd ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2022."

B. Updates by Drug

Table 2.--Notices of Updates to Recognized or Updated Susceptibility Test Interpretive Criteria by Drug[1]

Drug	Route of Administration	Action Taken	Therapeutic Category	Date
Amoxicillin and clavulanate	Oral	FDA does not recognize M100 standard and provides susceptibility test interpretive criteria for *Haemophilus influenzae*.	Antibacterial	5/17/22
Cefadroxil	Oral	FDA removed the statement "*Susceptibility of Enterobacteriaceae to cefadroxil may be deduced from testing cefazolin*." (Rationale available at	Antibacterial	4/27/22

		https://www.fda.gov/drugs/development-resources/rationale-fdas-position-cefadroxil.)		
Cefazolin	Injection	FDA does not recognize M100 standard for cefazolin as a surrogate to predict susceptibility of oral cephalosporins when used for the treatment of uncomplicated urinary tract infections caused by *Escherichia coli*, *Klebsiella pneumoniae* and *Proteus mirabilis*. (Rationale available at https://www.fda.gov/drugs/development-resources/rationale-fdas-position-use-cefazolin-breakpoints-surrogate-determining-breakpoints-oral.)	Antibacterial	10/20/22
Cefoxitin	Injection	FDA recognizes M100 standard for *Staphylococcus aureus* complex and *Staphylococcus lugdunensis*. FDA recognizes M100 disk diffusion standard for *Staphylococcus epidermidis* and other Staphylococci spp.	Antibacterial	10/4/22
Ceftolozane and tazobactam	Injection	FDA recognizes M100 disk diffusion standard for Enterobacterales.	Antibacterial	5/17/22
Lefamulin	Oral, Injection	FDA does not recognize M100 disk diffusion standard and provides susceptibility test interpretive criteria for *Streptococcus pneumoniae* and *Haemophilus influenzae*.	Antibacterial	5/17/22
Oxacillin	Injection	FDA concurs with the revised CLSI susceptibility test interpretive criteria for *Staphylococcus* by species level. (Rationale available at https://www.fda.gov/drugs/development-resources/rationale-fdas-position-oxacillin-breakpoints-staphylococcus). FDA references Cefoxitin susceptibility test interpretive for *Staphylococcus* spp. as a surrogate test.	Antibacterial	10/4/22
Piperacillin and tazobactam	Injection	FDA does not recognize M100 standard for Enterobacterales.	Antibacterial	5/17/22

[1] M100 standard in the table refers to CLSI Performance Standards for Antimicrobial Susceptibility Testing, 32nd ed. CLSI supplement M100; 2022.

Dated: May 15, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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