

Ad Hoc Working Group on Surrogate Testing

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Charge to Ad Hoc Group

- Define what is meant by surrogate testing
- Gather information on older and new uses of surrogate test markers
- To the extent possible harmonize language and usage such as “or” and various comments in the documents

Recent Background

- Some drugs cannot be tested accurately by disk – dalbavancin, oritavancin, tedizolid
- Some drugs stick to plastic and cannot be tested by E test strips - dalbavancin, oritavancin, tedizolid
- For those that can be tested by E test, still need FDA clearance (RUOs?)

Can We Use Surrogate
Markers for Some of
These New Drugs?

Why Test a Surrogate?

- If testing the surrogate provides a more accurate answer than testing the drug of interest itself (cefoxitin for oxacillin)
- If the surrogate is generalizable to other drugs in the same class (amp for amox)
- If the surrogate is more readily available or **the drug of interest is not available**

Classic Examples of Surrogates

- Amp to represent amox
- Pen to represent other β -lactamase labile pens vs. Staphs
- Oxacillin to represent other semisynthetic pens vs. Staph
- Erythromycin to represent azith and clarith
- Tetracycline S to represent S to doxy and mino

Other Examples

- Cephalothin to represent other 1st gen cephs with Staphs
- Cefazolin to represent certain oral cephs vs. *E. coli*, *K. pneumo*, *P. mirabilis*
- Sulfamethoxazole to represent other sulfas
- Ampicillin to predict imipenem – *E. faecalis*
- *Pen S predicts S to other β -lacs - Strep*

Some Possible New Examples

- With staph and enterococci, vancomycin **susceptible** isolates are predictably susceptible to dalbavancin, oritavancin, and telavancin
- Linezolid S = tedizolid S
- Footnotes could be added to antibiograms or even to lab reports

Proposed Definition

A surrogate drug can be defined as one that will accurately predict the susceptibility and/or resistance of another antimicrobial agent. Surrogate drugs may predict susceptibility only, resistance only, or both susceptibility and resistance. A surrogate susceptibility test may be useful in several settings.

- For efficiency, if one agent can be tested and those results accurately applied to other members of the same class it may preclude testing of several closely related agents (e.g., ampicillin to represent amoxicillin, penicillin G to represent other beta-lactamase labile penicillins with staphylococci)
- As indicated in some Tables in the document by the use of "or" between agents, cross susceptibility and resistance among some closely related agents is nearly complete (VME $< 3\%$; mE $< 10\%$) and only one agent need be tested.
- Testing a surrogate may provide more accurate prediction of susceptibility and resistance than testing the agent of interest itself (e.g., testing cefoxitin to predict susceptibility to oxacillin with staphylococci, testing pefloxacin and nalidixic acid to detect reduced fluoroquinolone susceptibility in Salmonella).
- Testing of a surrogate may be used to detect either susceptibility or resistance to closely related agents that may be technically difficult to test or for which reagents for testing are not readily available (e.g., tetracycline susceptibility to predict doxycycline or minocycline susceptibility with some species, using susceptibility to linezolid to predict susceptibility to tedizolid with some species).