Association for Molecular Pathology
Promoting Clinical Practice, Basic Research, and Education in Molecular Pathology
9650 Rockville Pike, Bethesda, Maryland 20814
Tel: 301-634-7939 ▪ Fax: 301-634-7990 ▪ Email: amp@asip.org ▪ *www.amp.org*

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Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Submitted electronically to: http://www.regulations.gov

To Whom It May Concern:

Thank you for the opportunity to submit comments on the draft guidance document entitled, "Establishing the Performance Characteristics of *In Vitro* Diagnostic Devices for the Detection of *Clostridium difficile.*" The Association for Molecular Pathology (AMP) is an international medical and professional association representing approximately 1,800 physicians, doctoral scientists, and medical technologists who perform laboratory testing based on knowledge derived from molecular biology, genetics and genomics. AMP commends the FDA on working to clarify the review requirements for *in vitro* diagnostics devices (IVDs) for *Clostridium difficile* (*C. difficile*); however, our members still find that aspects of the draft guidance document need further refinement and clarification. AMP's comments and recommendations are outlined below for your consideration.

General: AMP members are concerned that this guidance will increase the cost of assay development and that some of the new requirements may not be necessary to develop high quality assays.

Cross-reactivity: In regards for testing for potential cross-reactivity, the document needs to clarify if genomic DNA can be used and if bioinformatic data can be used to justify which specific strains are used as supporting data. Furthermore, in the case of assays only where analytical cross-reactivity is being assessed, why confirm a titer of each sample? Some of the organisms listed in Table 2 are fastidious and difficult to grow, which will unnecessarily increase time, effort and costs.

Within-Laboratory Precision/Repeatability: If the LoD studies of diverse species substantiates species-related reactivity differences, AMP recommends that the precision studies include additional strains beyond the 1-2 strains specified.

Confirmatory testing: The draft guidance document leaves questions about how to reconcile disparate results. For example, how are samples reconciled when the sample is cytotoxicity negative but PCR positive? Also, should the cytotoxicity testing encompass Toxin A, Toxin B and Toxin B variant if the NAT is detecting all three?

Study design: AMP encourages the FDA to clarify whether or not a checkerboard study is required if the instrument is already cleared or if this is specific for the assay.

Thank you for your consideration of AMP's recommendations and requests for further clarification. AMP members are available to offer their assistance to the FDA and please do not hesitate to contact us to discuss these comments as you work to finalize this draft guidance on IVDs for C. difficile.

Sincerely,

Elaine Lyon, PhD
Chair, Professional Relations Committee
amp@amp.org