

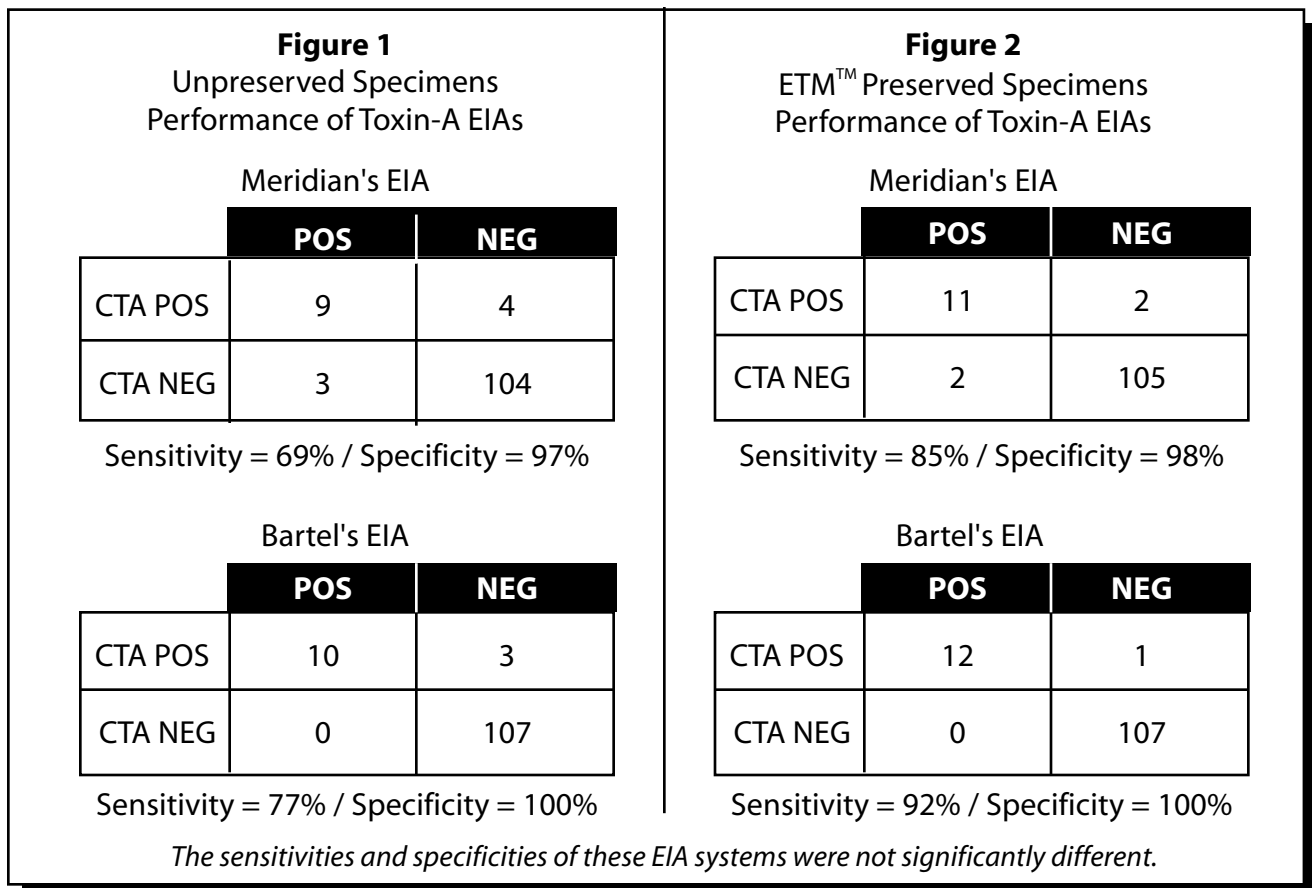
Cost Effective Laboratory Practices for the Detection of *C. difficile* Toxin

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Abstract

Today's volatile health care climate has put tremendous pressure on clinical microbiology laboratories to reduce costs and streamline testing. An algorithm we focused on is optimizing testing strategies for the detection of *Clostridium difficile* toxin (CDT). *C. difficile* is the most common cause of nosocomially acquired diarrhea. Rapid diagnosis is critical for the initiation of appropriate treatment regimens. This study was designed to 1) evaluate the utility of testing multiple specimens and 2) evaluate utilization of a stool transport media (ETM™ * Alpha-Tec Systems, Vancouver, Washington) for specimens collected at off-site locations (OSL), where transport to the lab can be delayed for up to 12 hours.

A total of 120 stools collected at OSL were tested in duplicate (one unpreserved and one preserved in transport media [ETM™]) by two Toxin-A EIA systems (Meridian [M] and Bartel [B]) and by a cytotoxicity assay (Bartel). The sensitivities of both EIAs for unpreserved stools were similar: 69% (M) and 77% (B). Delayed transport can result in degradation of toxin, thus requiring repeat testing. Sensitivities were higher for preserved stools: 85% (M) and 92% (B). Review of 477 stools demonstrated that testing multiple stools, particularly in one day, was not cost-effective. Eighty-three percent of patients testing positive for *C. difficile* toxin, which was diagnosed by the first stool tested. We recommend CDT testing be limited to one stool for the use of Alpha-Tec Systems ETM™ transport media.



* ETM™ is a trademark of Alpha-Tec Systems, Inc.

Summary of *C. difficile* Toxin-A results during a two-month retrospective review

Table 1

<i>C. difficile</i> EIA Result	Number of Specimens	Number of Patients
Toxin-A Positive	34	24
Toxin-A Negative	443	178
Total	477	202

Of 477 stool specimens tested, 7% were positive for *C. difficile* toxin.

Of 202 patients tested, 12% were diagnosed with *C. difficile*-associated diarrhea (CDAD).

The average number of specimens collected per patient was 1.4 for Toxin-A positive cases and 2.5 for Toxin-A negative cases.

Number of stool specimens submitted per patient

Table 2

Total Number of Stools Submitted	Number of Patients
1	94 (47%)
2	43 (21%)
3	30 (15%)
4	14 (7%)
5	4 (2%)
6	9 (4%)
≥ 8*	8 (4%)

* Four patients had 8 specimens each and 4 patients had 9, 10, 11 and 15 specimens each.

For the majority of patients (53%), multiple stool specimens were submitted for detection of *C. difficile* Toxin-A.

Analysis of stools submitted following initial Toxin-A negative specimen

Table 3

Number of Subsequent Stools	Number of Patients with All Toxin Negative Specimens	Number of Patients with ≥ One Toxin Positive Specimen
0	74	20
1	42	1 ¹
2	27	3 ²
3	14	0
4	4	0
5	9	0
≥ 7	8	0

- 1 Specimen two days after initial negative.
- 2 Specimen submitted 5, 7 and 11 days after initial negative.

Eighty-three percent of patients with *C. difficile* associated diarrhea were diagnosed on the basis of one specimen. An additional four patients were diagnosed with the second specimen submitted.

Utility of testing multiple specimens per patient collected within a 24-hour period

Table 4

Toxin-A EIA Results	Number of Patients with ≥ Two Toxin Specimen/Run	Number of Intra-Assay Discordants
Negative	40	0
Positive	4	0

Of the 202 patients analyzed during this study, 22% had two or more stool specimens tested for *C. difficile* Toxin-A during the same run. In all cases, there was complete intra-assay concordance among specimens.

Conclusions

1. The sensitivities of the Meridian and Bartels enzyme immunoassays designed to detect *C. difficile* Toxin-A are adversely effected by delays in transport and extended storage at room temperature.
2. Utilization of Alpha-Tec Systems' Enteric Transport Media (ETM™) resulted in enhanced detection of *C. difficile* Toxin-A when compared to stool specimens received via routine transport mechanisms. We recommend the use of Alpha-Tec Systems' ETM™ when receipt of the specimen in the laboratory is expected to be greater than two-hours after collection.
3. Although the majority of patients analyzed during this study had multiple specimens (range: 2 to 15) tested for *C. difficile* Toxin-A, 83% were diagnosed with CDAD with the first specimen. Therefore, we discourage the practice of testing more than two stool specimens within a 48-hour period.
4. The practice of sending multiple stools with a 24-hour period for *C. difficile* Toxin-A testing has become quite common, although studies validating this practice are lacking. We found no utility to testing multiple specimens from the same patient on the same day and have discontinued this practice.