In the recent paper of O’Connor et al. (1), four rapid methods for the detection of toxins of Clostridium difficile were evaluated. I have two main criticisms regarding the methodology of this study. First, for the different methods examined, the specimen treatment procedures were described as follows: for the culture procedure, “stool specimens were cultured on the day of receipt”; for the cytotoxicity evaluation, “a filtrate of each stool specimen was prepared and stored at −20°C”; and for immunological detection, “the stool specimen was frozen at −84°C until tested.” However, these three methods of sample preparation and treatment were compared with no obvious control.

Second, in the procedure described for the use of the rapid assay for the detection of toxin A from Oxoid Ltd., the paper states that for all methods used in the evaluation, “no rejection criteria were applied in respect of interval from collection to receipt of specimens,” but the Oxoid product instruction leaflet clearly states the following: “samples should be tested within 3 h of collection. If samples cannot be tested within this time, they should be stored in a refrigerator at 2 to 8°C and tested within 72 h.” The lack of regard for interval between specimen collection and receipt, together with the fact that specimens were frozen at −84°C until tested, leads me to conclude that the product instructions were not followed correctly in the evaluation of the Oxoid Ltd. assay.

The instructions for specimen collection and storage are given to help ensure that the clinical performance characteristics quoted in the leaflet are reliably met in the user’s laboratory. In part, the purpose of the development process pursued by responsible manufacturers of diagnostic kits is to design sample preparation procedures and test protocols that are not only convenient to the end-user but also robust. Ensuring that the correct result is obtained in the field is of paramount importance to us.

The work of O’Connor et al. raises issues for referees who consider papers describing the performance of commercially available products. I am sure that most kit manufacturers would be happy to supply copies of product instruction leaflets to enable referees to compare the use of the products by the authors with the instructions given by the manufacturers.

Given the above criticisms and the failure of the authors to determine the nature of the population, of the specimens tested, and of the test methodology used so that the reader can determine the nature of the population, of the specimens tested, and of the test methodology used so that the reader can form a judgment as to the validity of the conclusions and their applicability to the environment in which the reader works. We suggest that Dr. Hart’s ability to identify issues of concern to him in relation our results and conclusions is testimony to the quality of the review process in ensuring that all relevant issues were clearly presented in the paper.

REFERENCES

Don O’Connor
Microbiology Laboratory
Portiuncula Hospital Ballinasloe
County Galway, Ireland

Martin Cormican
Department of Bacteriology
Portiuncula Hospital Ballinasloe
County Galway, and
Department of Bacteriology
National University of Ireland
Galway, Ireland

Authors’ Reply

We thank Dr. Hart for his interest in our paper. Dr. Hart’s criticisms relate to two distinct issues. He is critical of the methodology of our study and also of the process of peer review as it was applied to the paper.

In relation to our methodology, the substance of Dr. Hart's objection is that the recommendations of the manufacturers of the Oxoid test were not fully complied with in that specimens received more than 3 h after collection were accepted for processing and in that specimens were stored frozen at −84°C prior to performance of the Oxoid Ltd. immunoassay test. Dr. Hart considers this as having resulted in an unfair evaluation of the Oxoid test system. We point out that the specimens evaluated in all four immunoassay systems were collected and stored in the same manner and that, notwithstanding this, the C. difficile toxin antigen(s) remained detectable in a number of the immunoassay systems. Dr. Hart is also concerned that we have not excluded the possibility that there are toxin A−B+ strains circulating in the population we serve. It appears that Dr. Hart feels that the Oxoid test system should be evaluated in a laboratory where specimens always arrive on time and where there is confidence that there are no toxin A−B+ strains in circulation, and it may be that in such an environment the Oxoid test would perform more satisfactorily. However, our laboratory serves several geographically dispersed hospitals, and specimens are not infrequently delayed for more than 3 h before receipt in the laboratory. Therefore, we believe that our conclusion that the Oxoid test is “unsuitable for use as an isolated test in our patient population” (1) is justified. Fortunately, some immunoassay systems appear to perform satisfactorily in such circumstances and we suggest that a manufacturer would do better to ensure that its test system works in diverse environments rather than chide clinical microbiology laboratories for being unworthy of its test.

In relation to the review process and the responsibilities of researchers in presenting their findings, we entirely reject the concept that research related to a commercial product must be performed on the terms of the manufacturer’s package insert. We consider it our responsibility, as well as that of the reviewers, to ensure, insofar as it is possible, that the reader can determine the nature of the population, of the specimens tested, and of the test methodology used so that the reader can form a judgment as to the validity of the conclusions and their applicability to the environment in which the reader works. We suggest that Dr. Hart’s ability to identify issues of concern to him in relation our results and conclusions is testimony to the quality of the review process in ensuring that all relevant issues were clearly presented in the paper.