agreement with Joshi et al.[1] In our article[3] we did not mention our clinical decision making for positive values near the cutoff value. Many of our clinical decisions were treated with caution when interpreting interferon-γ values in the range of 0.35 and 1.0 IU/mL. At our center, we suggested repeating the testing with QFT-GIT if the result was between 0.35 and 1.0 IU/mL.

The next question would be, What is the upper limit for the borderline zone? Herrera et al[4] did a study looking at the probability of a positive result if the QFT-GIT test is repeated. The data showed that if the interferon-γ value is between 0.35 and 0.7, the probability is 60%; if 0.7 to 1, it is 75%; if 1 to 2, it is 80%; and if greater than 2, it is 99%. With this data we agree to have a borderline zone between 0.35 and 2 IU/mL.

Our concept for proposing to raise the cutoff value for low-risk groups is similar to tuberculin skin test cutoff values for different risk populations. This possibility should be determined by future studies. At the present time we agree that a borderline zone of 0.35 to 2 IU/mL can be considered with cautious clinical interpretation when QFT-GIT is used for screening HCWs in low tuberculosis-prevalence areas.

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Consistency versus Accuracy in Reporting Central Line–Associated Bloodstream Infections

To the Editor—The commentary by Sexton et al[1] reflects the sentiment of our infection prevention department. We believe that accuracy, based on sound clinical judgment, is important. Consistency that results in inaccurate data is counterproductive.

The goal of absolute consistency in reporting central line–associated bloodstream infections (CLABSIs) may well be unattainable. Some subjective judgment is inevitable, but it may often result in a judgment that is more clinically accurate.

In our institution, when a patient has (1) obvious signs or symptoms of infection at a site other than the blood but no positive culture result and (2) one or more culture-positive blood samples and (3) a central line, then we designate the blood infection as secondary to the infected site. This approach has been approved by our hospital epidemiologist and our infection prevention committee. We also acknowledge instances of probable translocation.

With respect to skin contaminants, we have often had a culture-positive blood sample, not only with *Enterococcus* but also with a variety of other organisms that are known pathogens, without any concomitant signs or symptoms of sepsis. Consequently, we believe that essentially any organism could be a skin contaminant.

Credibility increases if clinicians perceive that data are based on sound clinical judgment. The designation of "indeterminate source" as proposed by Sexton et al[1] would result in CLABSI data that are both more consistent and more accurate. In addition to improving the quality of CLABSI data, adding an "indeterminate source" category would also allow better epidemiologic studies of these indeterminate patients, including determining who is at risk, thereby enabling us to legitimately broaden our understanding of what constitutes a potential contaminant.

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Toxin A–Negative, Toxin B–Positive *Clostridium difficile* Infection Diagnosed by Polymerase Chain Reaction

To the Editor—Clostridium difficile, the major cause of nosocomially acquired diarrhea and colitis, may produce 2 major virulence factors: toxin A and toxin B. The genes *TcdA* and *TcdB* are located in the same pathogenicity locus (PaLoc) and transcribed as 1 mRNA, so detection of toxin B alone by enzyme immunoassay is often used for diagnosis of *C. difficile* infection (CDI) regardless of its lower sensitivity and greater cost.[1] However, this approach fails to provide information as to whether toxin A is present or not. The presence of toxin A is important because toxin A^-B^+ *C. difficile* strains, such as ribotype 017, have been reported more frequently in Asia and Latin America than anywhere else.[2] Toxin A^-B^+ strains have been associated with higher rates of antibiotic resistance and may pose a great risk to patients.[3] The use of polymerase chain reaction (PCR) for the diagnosis of CDI is increasing because of its increased sensitivity and speed. For these reasons, the use of PCR methods that include the detection of *TcdA* genes is important for epidemiological surveys.

Recently, PCR methods have been used in some countries to conduct surveys of CDI.[2,5-7] In these surveys, we found that the rate of toxin A^-B^+ *C. difficile* strains differs significantly from region to region, ranging from 2.5% through 75%.[2,5,6] To make sure that the same PCR methods were used, we compared widely used primers, such as NK1–NK2, NK2–NK3, NK104–NK105, and A1C–A2N, used to conduct epidemic surveys in Japan, France, Argentina, and other countries. We found that isolation rates of toxin A^-B^+ *C. difficile* differ widely between Europe and Asia, that the PCR primers for *TcdA* from different countries are not uniform, and that the molecular criteria for *TcdA*-negative *TcdB*-positive strains need to be improved. These findings may explain why there are differences in the isolation rates of toxin A^-B^+ strains among different geographic regions.

We performed bioinformatic and comparative genome analysis on the primer regions of 7 published *C. difficile* sequences while looking for genomic sequence variations. In our analysis, primers M68 and CF5 belong to toxin A^-B^+, and others belong to the toxin A^+B^+ group (Figure 1). The PaLoc sequences of CF5 exhibit only 1 base pair difference from those of M68. However, the intergroup of toxin A^+B^+ and the intragroup between toxin A^+B^+ and toxin A^-B^+ show more diversity in the PaLoc region. These diversities, or single-nucleotide polymorphisms (SNPs), that occur in primers may weaken our signal when we use PCR methods to detect *TcdA/B* regions. For *TcdB*, NK104 and NK105, designed by Kato,[6] are widely used for detection. Their amplicons are located between the 2 highly variable regions of the 7 strains sequenced via SNP analysis and may explain their worldwide utility. However, we still found 3 sites (NK104, T17C, C26T; NK105, C20T) with apparent mutations among the 7 genomes (Figure 1).

Although the *TcdA* gene is conserved in the toxin A^-B^+ group, some papers have still found that these isolates have structural variation in the 3′ end of the gene, with the deletion of 600–1,700 base pairs.[5,8] Two or 3 pairs of primers (NK1, NK2, NK3, NK9, NK11, A1C, A2C, A3C, A2N, A3N, A4N) for each have been reported across this deletion region that can identify *TcdA* variation by the presence and size of their amplicons.[9] Among these primers, we found 7 sites (Figure 1*B*) with mutations in NK2–NK3 and A4N in the public genome that may cause a false negative result for toxin A^-B^+ strains when these regions are used for primers. We did not find mutations in any other primer regions. Thus, if we wish to simplify the process to detect toxin A, then primers A3C and A4N might be recommended to improve primer design.[5] We also advise using the downstream A4N position, which is closer to or beside the *TcdC* region, for lower SNP frequency. From SNP analysis of 7 known sequences, we can assert that the SNP in *TcdA* shows less diversity than that in *TcdB*, in addition to structural variation, and that primer design in different regions is based on the diversity of actual geographic strains. Proper primer design for *TcdA* should make the epidemiological data more accurate.

In conclusion, our group compares the primers for detection of toxins A and B from different regions via genome comparison and bioinformatics analysis. We found two gaps in current toxin A/B PCR detection, the toxin A^-B^+ strain isolation rate in Asia and North America and the different toxin A/B loci in different regions. According to these findings, we would advocate the establishment of a unified primer and method for toxin detection in different geographical regions. A unified approach should allow appropriate interpretation of the distinctly higher toxin A^-B^+ rates in Asia and Latin America. We also propose that the diverse *C. difficile* genomes found in different parts of the world be used to design primers for epidemiological surveys instead of existing primers that can give false negative results. Finally, we provide advice on the design of *TcdA* primers that we will apply to epidemiological surveys in Chinese hospitals in the near future.