False-Positive HIV-1 Test Results in a Low-Risk Screening Setting of Voluntary Blood Donation

Steven Kleinman, MD; Michael P. Busch, MD, PhD; Lisa Hall, MA; Ruth Thomson, MPH; Simone Glynn, MD, MPH; Dan Gallahan, PhD; Helen E. Ownby, PhD; Alan E. Williams, PhD; for the Retrovirus Epidemiology Donor Study

Context.—Persons at risk of human immunodeficiency virus 1 (HIV-1) infection have been classified incorrectly as HIV infected because of Western blot results, but the frequency of false-positive Western blot results is unknown.

Objectives.—To determine the frequency of false-positive HIV-1 Western blot results in US blood donors and to make projections to other screened populations. Secondly, to validate an algorithm for evaluating possible false-positive cases.

Design.—A retrospective cohort study of HIV-1 enzyme immunoassay (EIA) and Western blot results from large blood donor screening programs in which donors with suspected false-negative Western blot results underwent HIV-1 RNA polymerase chain reaction (PCR) testing and follow-up HIV-1 serology.

Setting.—Five US blood centers participating in the Retrovirus Epidemiology Donor Study.

Participants.—More than 5 million allogeneic and autologous blood donors who successfully donated blood at 1 of the 5 participating centers from 1991 through 1995.

Main Outcome Measures.—Rate of false positivity by Western blot and true HIV-1 infection status as determined by HIV-1 RNA PCR and by serologic follow-up of blood donors more than 5 weeks after donation.

Results.—Of 421 donors who were positive for HIV-1 by Western blot, 39 (9.3%) met the criteria of possible false positivity because they lacked reactivity to p31. Of these, 20 (51.3%) were proven by PCR not to be infected with HIV-1. The false-positive prevalence was 4.8% of Western blot–positive donors and 0.0004% (1 in 251 000) of all donors (95% confidence interval, 1 in 173 000 to 1 in 379 000 donors).

Conclusions.—A false diagnosis of HIV-1 infection can result from the combination of EIA and Western blot testing in blood donor and other HIV-1 screening programs. Individuals with a positive Western blot result lacking the p31 band should be counseled that, although they may not be HIV infected, there is uncertainty about this conclusion. These individuals should be further evaluated by RNA PCR testing (if feasible) and HIV serologic analysis on a follow-up sample.

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THE DIAGNOSIS of human immunodeficiency virus 1 (HIV-1) infection is made based on the detection of antibodies to HIV-1. This involves a 2-stage process beginning with a screening enzyme immunoassay (EIA) followed by a supplementary test to confirm the specificity of the EIA result. The supplementary test that is most often used is the HIV-1 Western blot assay. Until the early 1990s, the minimal criteria for interpretation of a Western blot result as positive were not standardized and at least 3 different Western blot interpretation schemas were in widespread use in varied screening and diagnostic settings.1,4 Because of concerns about possible false-positive reactions, the Food and Drug Administration (FDA) criteria used in the blood donor setting for a positive Western blot result interpretation required the detection of bands of 3 specific HIV-1 gene products: a core (Gag) protein (p24), an envelope (Env) glycoprotein (gp41 or gp120/160), and a polymerase protein (p31; endonuclease).4

In February 1993, the FDA made a set of recommendations for Western blot interpretation that were adopted by manufacturers of FDA-licensed HIV-1 Western blot kits. These less stringent criteria were adopted to reduce the number of HIV-1 seroindeterminate Western blot interpretations, particularly in high-risk screening settings, in which HIV-1–infected persons presenting during early seroconversion or with late-stage AIDS could be classified as seroindeterminate rather than as HIV-1 seropositive.5,6 The 1993 FDA-revised criteria for a positive Western blot result dropped the requirement for p31 reactivity. These new criteria stated that a result would be interpreted as HIV-1 Western blot positive if antibodies existed to 2 of the 3 diagnostic HIV-1 proteins: p24, gp41, and gp120/160.5,6

Since adoption of these revised criteria, several studies have identified low-risk individuals who have been falsely classified as HIV-1 infected as a result of positive HIV-1 Western blots because...
of Env-only (gp41 plus gp120/160) or Gag plus Env (p24 plus gp41 and/or gp120/160) patterns. One report described blood donors with HIV-1 Env-only patterns who lacked HIV risk factors and appeared not to be infected with HIV. Subsequently, Sayre et al reported 4 donors with similar positive Western blot patterns in whom follow-up testing did not show the development of additional Western blot bands that would be expected in seroconversion. These donors lacked HIV risk factors and had negative test results by HIV-1 RNA and DNA polymerase chain reaction (PCR) and by HIV-1 p24 antigen testing and HIV culture when performed.

To investigate the prevalence of false-positive HIV-1 Western blots, we reviewed a large blood donation database and systematically studied all anti-HIV EIA repeat-reactive Western blot-positive donations lacking the p31 band. Our purpose was to determine the frequency of false-positive HIV-1 Western blots in US blood donors, to validate an algorithm for selecting possible false-positive cases for further evaluation, and to determine those Western blot patterns most predictive of false-positive results.

**METHODS**

The Retrovirus Epidemiology Donor Study (REDS) is a study of viral infection in blood donors, conducted by 5 participating blood centers (Irwin Memorial Blood Centers, San Francisco, Calif; Oklahoma Blood Institute, Oklahoma City; and the Chesapeake-Potomac [Baltimore, Md], Southeastern Michigan [Detroit], and Southern California [Los Angeles] Regions of the American Red Cross), a coordinating center (Westat Inc, Rockville, Md), and a central laboratory (SRA Technologies, Rockville). As an element of REDS, anti-HIV EIA and Western blot results, including detailed band pattern data, are forwarded from all blood centers to the coordinating center and are maintained in a centralized database. Institutional review board approval for this aspect of REDS was received from all participating blood centers.

We reviewed the Western blot band patterns of all anti-HIV EIA repeat-reactive Western blot-positive donations from 1991 through 1995 using both computer records and source laboratory documentation. All donations included in this analysis were initially screened by either the Abbott (Abbott Park, Ill) anti-HIV-1 EIA (through March 1992) or the SRA Technologies anti-HIV-1/HIV-2 EIA (after March 1992). Enzyme immunoassay repeat-reactive samples were further tested with the FDA-licensed Biotech (Rockville, Md) Western blot.

Donations collected at Irwin Memorial Blood Centers from January 1991 through February 1992 were excluded from analysis because a different confirmatory test was used. For purposes of this analysis, we applied the 1993 revision of Western blot interpretive criteria to all donations in the 5 years of this study. We selected those positive Western blot results that completely lacked p31 reactivity (ie, absence of even +/- reactivity) for further investigation and used 2 separate methods to assess whether HIV infection was present. The first method was to test the results of any follow-up anti-HIV testing (EIA and Western blot) obtained as part of routine donor notification and counseling procedures. A nonseroconverting follow-up serology was defined as either negative anti-HIV EIA results or the lack of development of a p31 band on Western blot to conform with the pre-1993 positive interpretive criteria (p24, p31, gp41, or gp120/160) on a sample collected more than 5 weeks after the index donation. The second method was to test a frozen serum aliquot of the initial Western blot–positive donation for HIV-1 RNA by PCR assay at our central laboratory. In 2 cases, testing of follow-up rather than index donations was performed because of lack of sample availability. For PCR testing, we used the FDA-licensed Roche Amplicor HIV RNA assay (Roche Molecular Systems, Somerville, NJ) modified to yield qualitative rather than quantitative results. The modification used only the undiluted PCR-amplified product for probe hybridization and detection. Each assay included the kit internal standard spiked into each test sample prior to RNA extraction to control for RNA recovery, amplification efficiency, and assay inhibitors. To control for possible errors in PCR testing, we tested a second aliquot from the same donation (or from a subsequent donation from the same donor) in an independent PCR run for those donations in which there was either no follow-up sample for serologic testing or initial PCR results and follow-up serology suggested a conflicting interpretation of HIV infection status. The sensitivity and specificity of our modified PCR assay were evaluated on a panel of 100 frozen blood donor samples consisting of 50 anti-HIV EIA-negative samples and 50 anti–HIV-1 Western blot–positive samples with p31 reactivity. Using this sample set, the specificity of this assay was 100% and the sensitivity was 93% according to the modified assay sensitivity by comparing the performance of our modified assay with that of an FDA-licensed RNA PCR assay on 30 masked samples from 6 commercially prepared HIV-1 seroconversion panels. The modified PCR assay showed equivalent sensitivity to that reported by the panel manufacturer for the unmodified FDA-licensed assay. Results were identical in 29 of 30 samples; the result for the remaining sample, collected prior to HIV-1 antibody seroconversion, was indeterminate on the modified assay and negative on the licensed assay.

We calculated 95% confidence intervals (CIs) around prevalence estimates using a binomial distribution. Statistical testing was 2-tailed.

**RESULTS**

A review of the 5.02 million donations in the 1991-1995 REDS donation database revealed that 4650 were anti-HIV EIA repeat-reactive and 421 were HIV-1 Western blot positive (0.0086% of all donations; 0.006% of EIA repeat reacters) using the 1993 FDA interpretive criteria. Thirty-nine (9.3%) of the Western blots with positive results lacked the p31 band. We calculated 95% confidence intervals (CIs) around prevalence estimates using a binomial distribution. Statistical testing was 2-tailed.

**Table 1.—Classification of 39 Human Immunodeficiency Virus 1 Western Blot–Positive Samples Lacking p31 Reactivity**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Follow-up Serology*</th>
<th>RNA PCR Result†</th>
<th>No. of Samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>False positive</td>
<td>Non-Sc [Ellipses]</td>
<td>Negative[¶]</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Sc [†]</td>
<td>Negative[¶]</td>
<td>4</td>
</tr>
<tr>
<td>True positive</td>
<td>Sc</td>
<td>Positive [¶]</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>. . . . . . . . . . .</td>
<td>Positive [¶]</td>
<td>7</td>
</tr>
</tbody>
</table>

*Non-Sc indicates negative enzyme immunoassay or lack of Western blot p31 reactivity at more than 5 weeks follow-up; Sc indicates development of Western blot p31 reactivity (+/- other bands).
†RNA polymerase chain reaction (PCR) was performed on a frozen serum aliquot from index donation (or follow-up sample if index donation was unavailable).

Two donors developed a p17 band but no p31 band on 14-week follow-up.

One donor had a negative serology at 3 weeks but no sample at more than 5 weeks.

Ellipses indicate test not done.

PCR chain reaction repeated on 2 separate aliquots in 2 independent runs in 9 of 12 cases.

**One donor had a negative serology at 2 weeks but no sample at more than 5 weeks.**

**One donor had a negative serology at 2 weeks but no sample at more than 5 weeks.**
for 15 donors were identified as false positive based on a negative PCR assay in association with absence of progressive seroconversion on follow-up serology; in 5, the follow-up sample showed negative EIA results, and in 10, the Western blot showed absence of p31 reactivity. When compared with the index Western blot, the follow-up Western blot showed loss of reactivity to at least 1 HIV-1 antigen in 7 cases and no change in 2 cases. In a donor with an initial Western blot band pattern of gp41 plus gp120/160, an additional p17 band was reported in a 14-week follow-up sample, but no p31 band or additional bands were detectable on follow-up and the PCR result was negative. Two of these 15 cases were initially considered to have positive PCR results; however, the discrepancy with follow-up serology prompted repeat PCR testing. In 1 case, the PCR result was positive on repeat testing of the index donation but negative for the follow-up donation; in the second case, the PCR result was negative on repeat testing of the index donation and for the follow-up donation. Sample mix-up was excluded by performing HLA class II DR typing for 19 alleles using PCR on initial and follow-up repository samples in both cases; these results established donor identity in each case.

Results for 19 donations were classified as HIV-1 Western blot true positive (ie, donor infected with HIV-1); 7 based on a positive PCR result alone and 12 based on a positive PCR result and positive follow-up serology. In 7 of the 12 donors with follow-up serology, samples were available at an interval of 2 to 4 weeks after index donation; 6 of these 7 early follow-up samples showed p31 reactivity.

Table 2 relates the false-positive or true-positive Western blot classification of the 39 donors to the Western blot band pattern seen with the index donation. In addition to reactivity to Env antigens (gp41, gp120/160), reactivity to a maximum of 5 additional viral bands was possible (p17, p24, p51, p55, and p66) at the time of index donation. Results for the 5 samples with index donation patterns of Env bands only were all classified as Western blot false positive. Results for 13 of 15 samples with Env plus 1 additional viral band (9 with p24 reactivity, 3 with p66 reactivity, and 1 with p17 reactivity) were also false positive. In contrast, there were 2 false-positive results among 7 samples that contained Env plus 2 additional viral bands and no false-positive results in 2 samples that contained 3 additional bands or among the 10 samples that contained 4 or 5 additional bands.

The rate of false-positive Western blot results documented in this study was 0.00041% of all donations tested (95% CI, 0.00026%-0.00056%) and 4.8% of donations with results classified as Western blot positive. Prevalence was 5.5 times higher in donations from first-time allo- geneic donors (8/836,382 [0.00096%]) than in donations from repeat allogeneic donors (11/3,983,824 [0.00028%]). The prevalence ratio of false-positive Western blot results in first-time vs repeat donations was 3.46 (95% CI, 1.39-8.61). Of the 19 HIV-1 false-positive classifications in allo- geneic donors, 6 occurred in donations originally screened with the Abbott anti–HIV-1 EIA (prior to March 1992) and 13 in donations screened with the Abbott anti–HIV-1/HIV-2 assay. The rate of false-positive Western blot results using the anti–HIV-1/HIV-2 screening assay (0.00057%) was not statistically different from that using the anti–HIV-1/HIV-2 assay (0.00034%). The prevalence ratio of screened anti–HIV-1 vs anti–HIV-1/HIV-2 Western blot false-positive donations was 1.65 (95% CI, 0.63-4.35).

The results for 5 of 6 possible false-positive donations from autologous donors were found to be true positive (ie, donors were HIV infected). In 2 of these cases, the positive autologous donation was preceded by an autologous unit given 1 week previously. In 1 case, the autologous donor had given a previous donation that tested anti–HIV-1 EIA negative, and in the second case, the preceding autologous unit was HIV-1 EIA repeat reactive and Western blot indeterminate. The predictive value of a positive Western blot pattern lacking p31 for predicting HIV infection was 83% in autologous donors (95% CI, 42%-95%) but only 42% in allogeneic donors (95% CI, 28%-58%; 14 of 33 were HIV infected). These results were not statistically different (P = .09 by the Fisher 2-tailed exact test).

Incidence of HIV infection in other medical or public health HIV screening settings would be expected to be higher than that in allogeneic blood donors. Thus, the frequency of HIV infection presenting with a positive Western blot result lacking p31 should also be higher in such settings. Our data illustrate this by documenting a 9-fold higher frequency of HIV infection presenting with a Western blot lacking p31 in autologous donors (who are not subjected to predonation HIV risk factor screening) than in allogeneic donors (who are questioned about HIV risk factors) (0.00253% vs 0.00029%, respectively). Our data also show a difference in the positive predictive value (PPV) of a positive Western blot result lacking p31 reactivity for predicting HIV infection in these 2 donor populations (89% in autologous donors vs 42% in allogeneic donors); this difference is clinically relevant, although it does not achieve statistical significance, probably because of the small sample size of only 6 Western blot–positive autologous donors.

Table 3 illustrates how the PPV of Western blot patterns lacking p31 can be estimated if incidence of new HIV infection is known. In the table, we assume that the rate of false-positive results, which is a consequence of assay performance characteristics, will be similar in first-time blood donors and in higher-risk populations. An illustrative example from Table 3 shows that if incidence of HIV-1 infection in a particular screening setting is greater than 1% (as in anonymous testing clinics in San Francisco or in gay men presenting to sexually transmitted disease clinics), the PPV of a positive Western blot result lacking p31 will be greater than 99%. It has recently been estimated that the incidence of HIV infection in heterosexuals in the United States is 0.5%, which would result in a PPV of 98% in this population. A documented HIV infection incidence of less than 0.1% has been reported in heterosexuals presenting to sexually transmitted disease clinics in some communities; in these settings, the PPV drops to less than 91%. The PPV of 48.7% shown in Table 3 for a high-risk donor population is close to the 42% seen in our study.

Information on HIV risk factors was obtained during the course of postdonation counseling from some of the donors.
Nine of the 14 HIV-infected donors for whom risk factor information was available reported probable or definite HIV exposure risk. One of 7 donors with false-positive results for whom risk factor information was available reported HIV infection risk behavior. Two donors had received an experimental HIV vaccine as part of a research protocol and showed a pattern of reactivity to HIV glycoprotein antigens consistent with an antibody response to an Env subunit vaccine.

**COMMENT**

Individuals with new HIV-1 infection may donate blood or present at a screening clinic at a time when their antibody response to HIV-1 is in the early stages and is limited to Env-only or Env plus p31 reactivity on Western blot. It has been well established that persons undergoing HIV-1 seroconversion will rapidly develop reactivity to most, if not all, of the 9 HIV-1 antigens present on the Western blot strip. In this study, in a few cases for which early follow-up samples were available, we found that p31 reactivity could be seen as early as 2 weeks following results showing a Gag plus Env pattern. In a larger study, it has been estimated that the mean interval from detectability of a positive Western blot result by current FDA criteria to detectability using previous FDA criteria (ie, presence of the p31 band, which is usually the most delayed finding) is 35 days (range, 23-47 days).16 During HIV-1 seroconversion, high serum or plasma levels of HIV-1 RNA are present and the PCR assay used in this study has previously been shown to be sensitive enough to detect HIV-1 RNA when p31 reactivity is absent on Western blot.10,17

We used a combination of these 2 proven methods (follow-up serology and RNA PCR) to establish HIV infection status in 39 blood donors with possible false-positive Western blot results. All 27 donors who were assessed by evolution of Western blot patterns and by RNA PCR had concordant results (after PCR was repeated in 2 donors), strengthening our confidence in their classification. To ensure accurate classification of donors who lacked follow-up serologic data, PCR testing was carried out in 2 independent runs on 2 separate frozen aliquots in 8 of 11 such cases for which sufficient samples were available. In all 8 cases, the results were concordant with those of the original PCR assay. The initially positive PCR findings in 2 donors determined to be HIV uninfected on follow-up are most likely explained by contamination of the frozen aliquot subsequent to serologic testing but prior to PCR testing in one case and by a false-positive PCR assay result due to the presence of other PCR-positive samples in the same run in the second case.

The same Western blot patterns that are detectable in early seroconversion can also be seen in persons with false-positive results due to cross-reactivity with an epitope on gp41, which can give rise to multiple Western blot Env bands and a positive Western blot interpretation.8,9,18,19 This cross-reactivity to Env glycoprotein may be accompanied by a second nonspecific cross-reaction to p24 or other HIV proteins. Although most false-positive findings in our study are attributable to this mechanism, we also identified 2 donors in whom Western blot reactivity to HIV Env glycoproteins was probably a result of a true biological antibody response to an experimental Env subunit HIV vaccine. This mechanism of HIV false positivity may become increasingly significant if experimental HIV vaccination programs become more widespread.20 If HIV vaccination programs become routine, it will be important to develop HIV donor screening strategies that discriminate between HIV-infected persons and HIV-vaccinated, uninfected persons. Until such assay development occurs, it is important that HIV vaccine recipients be advised not to donate blood.

In this study, 20 (4.8%) of 421 EIA repeat-reactive, Western blot–positive donations occurred in donors who were not infected with HIV-1. Infection with other HIV variants (eg, HIV-2 and HIV-1 group O) is extremely rare in the United States and is highly unlikely in these donors, since none were born in African countries in which these variants are endemic.21,22 Also, the routine blood bank confirmatory testing algorithm in place since March 1992 has ruled out HIV-2 infection in the 14 donors with false-positive results detected by the anti–HIV-1/HIV-2 EIA (data not shown). Twenty (51.3%) of 39 donors and 19 (57.6%) of 33 allogeneic donors with positive Western blot results lacking p31 reactivity were not infected with HIV. When these 20 false-positive results were divided by the more than 5 million donations in our database, we calculated that 0.0004% or 1 in 251 000 donations were classified as HIV-1 infected based on false-positive Western blot results (95% CI, 1 in 173 000 to 1 in 579 000). When the prevalence of false positivity was calculated for first-time donors (who, to our knowledge, were not previously screened for HIV antibody), the rate increased to 0.00096% (1 in 104 547; 95% CI, 1 in 58 000 to 1 in 210 000). When multiplied by the 12 to 14 million annual whole blood donations in the United States, our data suggest that from 48 to 56 blood donors annually are misclassified as HIV-1 infected based on a combination of false-positive EIA and Western blot results.

In this study, all 5 donors who showed reactivity only to Env were not infected with HIV-1. However, a pattern of Env plus 1 other viral band reactivity was more frequently associated with false-positive results than was reactivity to
Env alone (18 vs 5 cases). Our data show that as the number of detectable bands increases, it is less likely that the observed pattern is a false-positive reaction and more likely an immune response to HIV infection. Nevertheless, the most inclusive algorithm for identifying potentially false-positive Western blot results is to flag all positive Western blot results completely lacking a p31 band (ie, not present even at weak or +/− strength) as requiring investigation. Implementation of this algorithm requires that the laboratory reporting the Western blot results specify the Western blot bands identified. Appropriate personnel at the testing laboratory, the blood center, or the screening clinic should review the laboratory reports and separate Western blot–positive persons into those who show an unambiguous positive result pattern and those who have a possible false-positive result.

In high-risk screening settings (ie, HIV infection incidence >0.5%), the counseling message concerning a positive Western blot result lacking p31 reactivity should stress the high likelihood of HIV infection until refuted by additional test results. In lower-incidence settings, the counseling message may contain more uncertainty. We believe that all persons with positive HIV-1 Western blot patterns lacking p31 should be counseled differently than other Western blot–positive individuals. The counseling message should include the standard information given to all HIV-1 Western blot–positive persons but, in addition, should also indicate that the person’s pattern of HIV-1 reactivity has been found in persons who were and were not subsequently proven to be infected with HIV. Since the likelihood of false-positive results is dependent on the PPV in the screening setting as well as the specific Western blot band pattern, informed counselors can use this information to refine the counseling message for individual clients.

The importance of an additional laboratory sample to help resolve the person’s HIV status should be stressed. If resolution of HIV status is to be based on the development of additional Western blot reactivity (especially p31) on a follow-up sample, we suggest that this sample be obtained within several weeks of the initial laboratory test to allow for the possibility of rapid definitive diagnosis. Although the reported mean interval to development of p31 reactivity is 35 days after a positive Western blot finding, it may be possible to diagnose infection earlier as a result of a more rapid development of p31 reactivity (as was seen in several individuals in our study). Alternatively, HIV infection may be inferred if there is an increase in strength of Env reactivity in the follow-up sample, provided that both index and follow-up samples are assayed in parallel on a single Western blot run.

Due to potential biological variability in the kinetics of antibody formation, lack of development of p31 reactivity after several weeks does not rule out HIV infection. Thus, we agree with Centers for Disease Control and Prevention recommendations that indicate that a second follow-up sample needs to be obtained to definitively resolve HIV status. A follow-up interval of 6 months from date of first diagnosis is recommended if initial follow-up testing indicates lack of infection, whereas an 8- to 12-week interval is recommended if the initial follow-up indicated that infection is likely to be present. If the person has a risk factor for immunologically divergent HIV infection (ie, African birth or sexual or parenteral contact with a person born in Africa), consideration should be given to performing tests that will detect HIV-2 or HIV-1 group O infection.

These limitations suggest that a better method of evaluation might be to perform additional laboratory testing on the index donation sample. Data from seroconverting plasma donor panels showed that HIV p24 antigen was detectable in 38% of HIV-1–infected samples that lacked p31 on Western blot. Thus, the presence of p24 antigen can confirm that the positive Western blot result is associated with HIV-1 infection; in contrast, the absence of p24 antigen does not help resolve HIV status. Since March 1996, p24 antigen testing has been performed as part of routine blood donation screening; hence, these data are now routinely available for counseling currently tested donors. Because HIV RNA was detectable in 100% of these same plasma donor seroconversion samples, this suggests that a valid but still unproven approach to investigating the HIV infection status of persons with potentially false-positive Western blot results would be to obtain RNA PCR results on the index sample prior to initiating notification. A negative result would most probably rule out HIV infection, whereas a positive result would be highly suggestive of infection, provided this was not a consequence of a sample-labeling or cross-contamination problem. Our experience in this study, in which false-positive RNA PCR results were initially obtained in 2 of 38 donors, is supported by a recent report in which 1 of 20 samples from HIV-uninfected persons with problematic HIV PCR results showed a false-positive HIV PCR result. Thus, although in theory the PCR assay can conclusively establish HIV infection status, this has not yet been sufficiently validated in the diagnostic clinical laboratory setting to justify relying solely on such results. Some assurance against incorrect interpretation of PCR results might be provided by additional HIV-1 RNA PCR testing of a follow-up sample (in conjunction with follow-up HIV serology). Such dual-sample PCR testing would allow HIV infection to be ruled out with a greater degree of certainty than by follow-up serology alone and should permit shortening of the follow-up sampling interval required to rule out infection.

The misclassification of even 1 HIV-uninfected person as HIV infected has serious consequences for that person, their family, and the institution providing the notification. Because of the recognized potential for sample-labeling errors or sample contamination, the Association of State and Territorial Public Health Laboratory Directors, Washington, DC, has previously recommended that a follow-up sample be obtained to verify a person’s initial positive HIV-1 Western blot result. The recognition that false-positive HIV-1 Western blot results occur because of biological reasons in low-risk screening settings reinforces the need for institutions to follow this recommendation. It is likely that the testing and counseling procedures that we have suggested may be refined as more studies are performed and as PCR testing becomes more widely available and clinically validated.

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