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TRANSPLANT INFECTIOUS DISEASE

ORIGINAL ARTICLE

# Serological testing on the ADVIA Centaur system for human immunodeficiency virus, hepatitis B virus, and hepatitis C virus in specimens from deceased and living individuals demonstrates equivalent results[ǂ]

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## Abstract

**Introduction:** To determine the suitability of human tissues and cells for transplantation, guidelines mandate infectious disease testing of serum or plasma obtained from deceased donors, which are often collected after cessation of the heartbeat. Tests used for this purpose are required to show equivalent performance when compared to pre-mortem specimens. This study evaluated whether serology assays for HIV Ag/Ab Combo, hepatitis B virus (HBc Total; HBsAgII), and HCV on the ADVIA Centaur system, were fit for testing post-mortem sera. Performance evaluation studies included precision, specificity, and sensitivity.

**Methods:** Blood specimens were collected within 24 h after death from 82 deceased and 83 healthy living individuals. Studies followed standard guidelines. The 20-day precision study was performed on five levels of post-mortem specimens (non-spiked and spiked). The specificity study compared 81–83 pre-mortem and 74–82 post-mortem specimens. The sensitivity study compared 50 pre-mortem and 50 post-mortem specimens spiked with positive sera for each analyte at two levels to achieve a low (near cutoff) positive result and a second higher positive result.

**Results:** Precision, specificity, and sensitivity study results met acceptance criteria for all assays and lots; post-mortem and pre-mortem results were equivalent.

**Conclusion:** Based on this study, the ADVIA Centaur CHIV, HBcT, HBsAgII, and HCV assays are acceptable for use in routine testing of deceased donor sera collected after cessation of the heartbeat.

KEYWORDS
deceased donors, HBV, HCV, HIV, infectious disease, transplant

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## 1 | INTRODUCTION

The number of deceased tissue donors and transplantations has risen steadily in the past 10 years. Deceased individuals are the major source of tissues for transplants.[1] Tissue transplants include the cornea, bone, tendon, skin, heart valves, nerves and veins, and cell transplants include pancreatic islet cells, hematopoietic progenitor cells, and marrow.

Tissues from deceased individuals carry the risk of transmitting an unexpected infectious disease to allograft recipients. Although not common, donor-derived infections may lead to serious health complications and even death. Notable among infectious diseases are acquired immunodeficiency syndrome (AIDS) caused by the human immunodeficiency virus (HIV), hepatitis B caused by the hepatitis B virus (HBV), and hepatitis C caused by the hepatitis C virus (HCV). The screening of deceased donor blood using immunoassays that detect common infectious diseases can help minimize the transfer of infection to a healthy recipient. Whereas blood specimens for use in testing deceased organ donors are collected from heart-beating individuals, blood specimens for use in testing deceased tissue donors are often collected after cessation of the heartbeat. Most regulatory bodies do not make a distinction regarding requirements for assay validation between specimens obtained from heart-beating deceased donors and those from other heart-beating donors (i.e., living donors) – but rather, there are concerns about verifying assay performance in the altered blood matrix that occurs after cessation of the heartbeat. That is, sample quality is considerably different between samples collected after brain death and cardiac death. For example, after cessation of the heartbeat, alterations occur in the blood matrix due to multiple causes (autolysis, hemolysis, bacterial growth, hemodilution due to blood transfusion, etc.) and might lead to inaccurate (false-negative [FN] or false-positive [FP]) test results for some assays.

To address the potential risk of infectious disease transmission and to maintain tissue and cell quality and safety for donor selection, several countries have issued guidelines for donor selection, testing, handling, preserving, storing, and distribution of human tissues and cells.[2–9] Some countries require regulatory approval before a test can be used on post-mortem specimens.[4,6,7,10] Thus, immunoassays to be used for deceased donor screening after cessation of the heartbeat must be shown to be suitable for this intended use through appropriate performance validation studies using post-mortem serum or plasma. These validation studies should demonstrate that performance claims previously established using pre-mortem specimens are also met using post-mortem specimens.

In the European Union, assay systems must adhere to the requirements of the Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices.[11] If the intended use of assays does not include testing of post-mortem serum samples, validation studies are recommended for the release of tissues for transplantation. Assays for the detection of infections with HIV, HCV, and HBV must meet the Common Technical Specifications (CTS) [2009/886/EC] including sensitivity and specificity evaluation using serum and plasma. Validation studies are performed in individual laboratories. The Paul-Ehrlich-Institut (the German federal agency, medical regulatory body, and research institution) has proposed a validation study for serological assays using post-mortem specimens. Recommendations in the Paul-Ehrlich-Institut proposal and the 2004 US recommendations are similar.[2,12] In Australia, the Therapeutic Goods Administration (TGA) of the Department of Health and Aging requires that assays to be used for screening infectious diseases be acceptable by TGA and that assays and facilities performing the assays should also be approved by the country's regulatory authority for that purpose.[7] Other countries have similar guidelines.

The goal of this study was to evaluate the suitability of ADVIA Centaur assays to detect HIV, HBV, and HCV for screening post-mortem serum specimens (i.e., blood collected after cessation of the heartbeat) obtained within 24 h after death. Evaluations included precision, specificity, and sensitivity studies for specimens obtained from deceased and living donors as recommended by current guidelines.

## 2 | METHODS

### 2.1 | Specimen procurement

Post-mortem serum specimens (82) were obtained from Boca Biolistics (Pompano Beach, Florida, USA). These specimens were confirmed by the vendor to have been drawn within 24 h of time of death and were stored frozen at −20°C or lower for several months. Table 1 summarizes the characteristics of the donors. The mean age for deceased donors was 61.8 years (range 14–80 years); 59 were males and 41 were females. The longest time between death and blood draw was 1280 min (21.33 h). The shortest time was 62 min. The mean time was 627 min (10.45 h). Normal random living donor (pre-mortem) specimens (83) (non-reactive for all analytes tested in this study) were obtained by the National Serology Reference Laboratory (NRL) (Victoria, Australia) for comparison. Samples were thawed at 2–8°C for up to 48 h before testing. This retrospective study had relevant institutional agreements and donor consent for the prior collection of specimens.

### 2.2 | Immunoassays and testing

The ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay is for the detection of HIV p24 antigen and antibodies to HIV type 1, Including group O (HIV-1 + "O") and/or type 2 (HIV-2). The ADVIA Centaur HBc Total (HBcT) assay is for the detection of total antibodies to hepatitis B core antigen. The ADVIA Centaur HBsAgII (HBsAgII) assay is for the qualitative detection of hepatitis B surface antigen (HBsAg). The ADVIA Centaur HCV (HCV) assay is for the detection of immunoglobulin G (IgG) antibodies to HCV. The ADVIA Centaur HBsAg Confirmatory assay is an in vitro immunoassay for the qualitative confirmation of HBsAg (for use with the ADVIA Centaur HBsAgII assay). All assays were performed as specified in the individual instructions for use. Three routinely manufactured reagent lots of each assay were evaluated. Each assay reagent composition and test parameters were not altered. The standard calibrators, controls, and master curves were

**TABLE 1** Demographic characteristics of post-mortem and living donor specimens used for specificity and sensitivity studies

| | Post-mortem specimens (Boca Biolistics, USA) | Pre-mortem specimens (National Serology Reference Laboratory, Australia) |
|---|---|---|
| Number collected | 82 | 83 |
| Age, years | | ‡ |
| Mean (range) | 61.8 (14–80) | |
| Post-mortem time, h | < 24 | N/A§ |
| Mean (range) | 10.45 h (1h 2 min to 21.33 h) | |
| Sex | | ‡ |
| Male | 59 | |
| Female | 41 | |
| Race | | ‡ |
| Asian | 4 | |
| Black/African American | 8 | |
| Hispanic/Latino | 8 | |
| White/Caucasian | 62 | |
| Cause of death: | | N/A |
| Cardiopulmonary arrest | 3 | |
| Cancer | 10 | |
| Cardiac | 31 | |
| Cardiac arrest | 10 | |
| Cardiac event | 2 | |
| Cerebral vascular aneurysm | 2 | |
| End-stage liver disease | 3 | |
| End-stage renal disease | 1 | |
| Hanging | 1 | |
| Heart disease | 1 | |
| Intracranial bleeding (ICB) | 2 | |
| Intracranial bleeding/intracerebral hemorrhage (ICB/ICH) | 2 | |
| Overdose | 2 | |
| Pneumonia (PNA) | 1 | |
| Pulmonary embolism | 1 | |
| Respiratory | 1 | |
| Respiratory failure | 4 | |
| Ruptured aortic aneurysm | 1 | |
| Prescription overdose | 1 | |
| ST-segment elevation myocardial infarction | 1 | |
| Suicide | 1 | |
| Sensitivity study | | |
| n | 50 | 50 |
| Mean ± SD | 62.6 ± 9.9 | ‡ |
| Median (Interquartile range, IQR) | 65 (56–69.8) | ‡ |
| Range | 22–75 | ‡ |

(Continues)

**TABLE 1** (Continued)

| | Post-mortem specimens (Boca Biolistics, USA) | Pre-mortem specimens (National Serology Reference Laboratory, Australia) |
|---|---|---|
| Race | | ‡ |
| Asian | 4 | N/A |
| Black/African American | 3 | |
| Hispanic/Latino | 7 | |
| White/Caucasian | 36 | |
| Cause of death: | | |
| Cardiopulmonary arrest | 3 | |
| Cancer | 6 | |
| Cardiac | 12 | |
| Cardiac arrest | 10 | |
| Cardiac event | 2 | |
| Cerebral vascular aneurysm | 2 | |
| End-stage liver disease | 3 | |
| End-stage renal disease | 1 | |
| Heart disease | 1 | |
| Intracranial bleeding/intracerebral hemorrhage (ICB/ICH) | 2 | |
| Overdose | 2 | |
| Pneumonia | 1 | |
| Respiratory failure | 1 | |
| Respiratory | 1 | |
| Ruptured aortic aneurysm | 1 | |
| ST-segment elevation myocardial infarction | 1 | |
| Suicide | 1 | |
| Specificity study | | |
| Pre-mortem | | 81–83† |
| Post-mortem | 74–82† | |

†Precise number depended on the lot and assay. See Table 2.
‡Not available.
§N/A: Not applicable.

used for results generation. Testing was performed on a single ADVIA Centaur XPT system located at the NRL, Victoria, Australia, except for the HBsAg Confirmatory and HBcT2 assays which were performed at Siemens Healthineers (Tarrytown, New York, USA). (The HBcT2 assay was not commercially available in Australia at the time other assays were tested). Additionally, specificity results for the HBsAgII assay were reproduced at Siemens Healthineers because Lot 3 was short of samples by about 40%.

## 2.3 | Repeatability and within-lab precision

Precision: Repeatability and within-lab precision studies for ADVIA Centaur CHIV, HBcT, HBsAgII, and HCV assays were performed according to Clinical and Laboratory Standards Institute (CLSI) Document EP05-A3[13] using five sample pools prepared from post-mortem serum. The pools were divided into five levels for each analyte: one non-spiked and four spiked with high-titer positive serum for each infectious disease analyte to levels near cutoff negative, near cutoff positive, mid positive, and high positive. The resulting repeatability and within-lab percent coefficients of variation (%CVs) (or SDs) were evaluated against existing acceptance criteria for living specimens. Each study was performed over 20 days, with two replicates per sample in each of two runs per day for a total of eighty replicates per sample, per reagent lot. Each completed run was evaluated with two replicates from single aliquots of the following five samples for each of the assays: low negative; near-cutoff negative (spiked); near-cutoff positive (spiked); mid positive serum sample (spiked); high positive (spiked).

## 2.4 | Specificity

The specificity of the assays was evaluated by comparing the results of pre-mortem and post-mortem specimens.[10] Samples were collected from a minimum of 81–83 living donors and 74–82 deceased donors who had no previous diagnosis of HBV, HCV, or HIV. (The precise number depended on the assay and the lot; see Table 2). For each assay, all specimens were tested using each of three lots on one ADVIA Centaur XPT system. Any samples that were reactive with the assays were tested in duplicate with an additional validated commercially available method, and the resolved percent specificity was calculated for each population. Samples that were reactive on both the ADVIA Centaur assay and the resolution method were excluded from the final analysis. Six samples were reactive in the HBcT assay; four were designated TP based on results from the DiaSorin LIAISON XL platform and excluded from the dataset, resulting in 78 specimens. These four specimens were not excluded for CHIV, HBsAgII, and HCV assay testing. No other specimens were excluded from the study. Acceptance criteria required that the assay demonstrate no statistically significant difference ($p > 0.05$) between the resolved non-reactive determination of pre-mortem and post-mortem specimens.

## 2.5 | Sensitivity

Sensitivity of the ADVIA Centaur CHIV, HBcT, HBcT2, HBsAgII, HBsAg Confirmatory (for HBsAgII assay), and HCV assays was evaluated by comparing results of pre-mortem and post-mortem specimens.[10,12] Specimens were collected from 50 deceased and 50 living donors (unmatched) who had no previous diagnosis of HBV, HCV, or HIV. The demographics of the donors are presented in Table 1. Each pre-mortem and post-mortem specimen was split into two or more aliquots and spiked with the relevant disease-related analytes at two levels to achieve a low (near cutoff) positive result and a second higher positive result. Specimens were spiked over a couple of days and placed at −20°C. The time between completion of spiking and testing was 1 day for CHIV, 4 days for HBsAgII, 9 days for HBcT, and 8 days for HCV. For HBsAgII testing in Tarrytown, specimens were spiked over two days, placed at 2–8°C, and tested within four days. These samples were then frozen at −20°C for HBsAg Confirmatory testing. The HBsAg Confirmatory assay is a relatively complex assay that has a long time to result and requires two results for each sample to be confirmed. Because of this, HBsAg sensitivity samples were thawed, centrifuged, and tested in batches, so testing of the 200 samples took several days. For the HBcT2 assay, after characterizing the spikers through multiple dilutions, specimens were spiked in one day, refrigerated overnight (2–8°C), and tested the following day. Samples were assayed neat, prior to spiking analyte, to accurately determine the delta (change in index or concentration) between non-spiked and spiked samples. For each assay, a minimum of five individual positive sources from the NRL's sample bank was used for the spiking of samples. Spiking volume did not exceed one-tenth (10%) of the total sample volume. For each concentration, the mean value of results for the 50 post-mortem donor specimens was compared to the mean value of results for the 50 pre-mortem specimens using the following formula:

$$\%\text{Mean Difference} = 100 \times \left( \frac{\text{Mean Deceased Donor Index} - \text{Mean Living Donor Index}}{\text{Mean Living Donor Index}} \right)$$

Acceptance criteria required that assay percent difference between spiked pre-mortem and post-mortem specimens be within ±25.0%, following guidance from the Paul-Ehrlich-Institut as of 2014.[12] For the ADVIA Centaur HBsAg Confirmatory assay, confirmation of initially reactive samples had to agree 100% between spiked pre-mortem and post-mortem specimens.

## 2.6 | Accuracy

For accuracy, the 2004 USA and the 2014 Paul-Ehrlich-Institut proposal recommend testing of at least 20 pre-mortem and post-mortem specimens per analyte, each sample divided into at least three aliquots—one non-spiked and two spiked with an analyte in two different concentrations to check sensitivity (low and medium to high positive). The low positive aliquot should be near the cut-off (about 2- to 4-fold s/co ratio) and the medium to high positive aliquot should be within the linear measuring range of the assay. The spiking volumes should be no more than a tenth of the sample volume. Accuracy for testing of non-spiked samples was performed in the specificity section on >80 pre-mortem and >80 post-mortem specimens. Accuracy for testing of samples spiked to near the cutoff (limit of detection) and to higher detection levels was performed in the sensitivity section on 50 pre-mortem and 50 post-mortem specimens.

# 3 | RESULTS

Based on this study, precision, specificity, and sensitivity evaluations met acceptance criteria for all assays and lots evaluated.

## 3.1 | Precision

Table 2 summarizes the precision study results. For each assay tested, all three lots met acceptance criteria. For some low negative sample results, the "*n*" was less than 80. This was because some results were less than 0.0 Index and were not used in the precision calculations. For these samples, "*n*" is marked in Table 2. The 20-day CLSI precision protocol is routinely used to obtain precision data for ADVIA Centaur assays including all those used in this study. Using the 20-day CLSI protocol for post-mortem specimens and applying the same acceptance criteria as those used when performing a precision study with pre-mortem specimens allowed us to claim equivalent precision with high confidence for pre-mortem and post-mortem specimens.

**TABLE 2** Summary table of precision study for serum sample pools from deceased donors

| System: ADVIA Centaur XPT | | | | | Repeatability | | | | Within-lab precision | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Assay | Lot | Sample | *n* | Mean | SD | %CV | Acceptance criteria | Pass/fail | SD | %CV | Acceptance criteria | Pass/fail |
| CHIV | 1 | Low neg | 80 | 0.30 | 0.02 | 8.4 | NA | NA | 0.04 | 14.8 | NA | NA |
| | | Pos low p24 | 80 | 1.16 | 0.02 | 1.9 | ≤10% (%CV) | Pass | 0.11 | 9.4 | ≤15% (%CV) | Pass |
| | | Low pos HIV-2 | 80 | 1.59 | 0.03 | 1.9 | ≤10% (%CV) | Pass | 0.09 | 5.4 | ≤15% (%CV) | Pass |
| | | Low pos HIV-1 | 80 | 1.80 | 0.03 | 1.9 | ≤10% (%CV) | Pass | 0.09 | 5.3 | ≤15% (%CV) | Pass |
| | 2 | Low neg | 80 | 0.28 | 0.01 | 3.7 | NA | NA | 0.05 | 19.0 | NA | NA |
| | | Pos low p24 | 80 | 1.14 | 0.02 | 2.1 | ≤10% (%CV) | Pass | 0.11 | 9.3 | ≤15% (%CV) | Pass |
| | | Low pos HIV-2 | 80 | 1.56 | 0.03 | 1.9 | ≤10% (%CV) | Pass | 0.11 | 7.2 | ≤15% (%CV) | Pass |
| | | Low pos HIV-1 | 80 | 1.69 | 0.02 | 1.5 | ≤10% (%CV) | Pass | 0.13 | 7.9 | ≤15% (%CV) | Pass |
| | 3 | Low neg | 80 | 0.25 | 0.02 | 8.4 | NA | NA | 0.04 | 17.2 | NA | NA |
| | | Pos low p24 | 80 | 1.15 | 0.02 | 2.1 | ≤10% (%CV) | Pass | 0.10 | 8.6 | ≤15% (%CV) | Pass |
| | | Low pos HIV-2 | 80 | 1.33 | 0.02 | 1.6 | ≤10% (%CV) | Pass | 0.08 | 5.8 | ≤15% (%CV) | Pass |
| | | Low pos HIV-1 | 80 | 1.90 | 0.03 | 1.8 | ≤10% (%CV) | Pass | 0.13 | 7.0 | ≤15% (%CV) | Pass |
| HBcT | 1 | Low neg | 21[†] | 0.10 | 0.02 | 19.6 | NA | NA | 0.02 | 19.6 | NA | NA |
| | | Neg near co | 80 | 1.13 | 0.04 | 3.7 | ≤10% (%CV) | Pass | 0.08 | 7.3 | ≤15% (%CV) | Pass |
| | | Pos near co | 80 | 2.20 | 0.07 | 3.1 | ≤10% (%CV) | Pass | 0.11 | 4.9 | ≤15% (%CV) | Pass |
| | | Pos mid | 80 | 3.12 | 0.09 | 3.0 | ≤10% (%CV) | Pass | 0.13 | 4.3 | ≤15% (%CV) | Pass |
| | | Pos high | 80 | 6.04 | 0.15 | 2.5 | ≤10% (%CV) | Pass | 0.26 | 4.3 | ≤15% (%CV) | Pass |
| | 2 | Low neg | 47[†] | 0.15 | 0.03 | 17.3 | NA | NA | 0.06 | 38.7 | NA | NA |
| | | Neg near co | 80 | 1.11 | 0.04 | 3.2 | ≤10% (%CV) | Pass | 0.09 | 8.5 | ≤15% (%CV) | Pass |
| | | Pos near co | 80 | 2.08 | 0.06 | 3.0 | ≤10% (%CV) | Pass | 0.11 | 5.2 | ≤15% (%CV) | Pass |
| | | Pos mid | 80 | 2.94 | 0.08 | 2.8 | ≤10% (%CV) | Pass | 0.11 | 3.8 | ≤15% (%CV) | Pass |
| | | Pos high | 80 | 5.83 | 0.12 | 2.1 | ≤10% (%CV) | Pass | 0.18 | 3.1 | ≤15% (%CV) | Pass |
| | 3 | Low neg | 59[†] | 0.18 | 0.02 | 10.2 | NA | NA | 0.08 | 47.3 | NA | NA |
| | | Neg near co | 80 | 1.13 | 0.04 | 3.9 | ≤10% (%CV) | Pass | 0.12 | 11.0 | ≤15% (%CV) | Pass |
| | | Pos near co | 79 | 2.08 | 0.07 | 3.1 | ≤10% (%CV) | Pass | 0.17 | 8.3 | ≤15% (%CV) | Pass |
| | | Pos mid | 80 | 2.91 | 0.08 | 2.9 | ≤10% (%CV) | Pass | 0.19 | 6.6 | ≤15% (%CV) | Pass |
| | | Pos high | 79 | 5.58 | 0.19 | 3.3 | ≤10% (%CV) | Pass | 0.34 | 6.1 | ≤15% (%CV) | Pass |
| HBsAgII | 1 | Low neg | 9[†] | 0.16 | 0.00 | 0.0 | NA | NA | 0.00 | 0.0 | NA | NA |
| | | Neg near co | 80 | 0.82 | 0.06 | 7.4 | ≤12% (%CV) | Pass | 0.07 | 9.1 | ≤15% (%CV) | Pass |
| | | Pos near co | 80 | 1.64 | 0.10 | 5.8 | ≤12% (%CV) | Pass | 0.10 | 5.9 | ≤15% (%CV) | Pass |
| | | Pos mid | 80 | 2.89 | 0.11 | 3.9 | ≤12% (%CV) | Pass | 0.13 | 4.6 | ≤15% (%CV) | Pass |
| | | Pos high | 80 | 8.92 | 0.27 | 3.0 | ≤12% (%CV) | Pass | 0.29 | 3.3 | ≤15% (%CV) | Pass |
| | 2 | Low neg | 3[†] | 0.14 | 0.00 | 0.0 | NA | NA | 0.00 | 0.0 | NA | NA |
| | | Neg near co | 80 | 0.83 | 0.07 | 8.5 | ≤12% (%CV) | Pass | 0.08 | 10.2 | ≤15% (%CV) | Pass |
| | | Pos near co | 80 | 1.67 | 0.08 | 4.6 | ≤12% (%CV) | Pass | 0.08 | 4.9 | ≤15% (%CV) | Pass |
| | | Pos mid | 80 | 2.96 | 0.11 | 3.6 | ≤12% (%CV) | Pass | 0.11 | 3.8 | ≤15% (%CV) | Pass |
| | | Pos high | 80 | 9.17 | 0.21 | 2.3 | ≤12% (%CV) | Pass | 0.26 | 2.8 | ≤15% (%CV) | Pass |
| | 3 | Low neg | 14[†] | 0.11 | 0.01 | 4.5 | NA | NA | 0.02 | 14.6 | NA | NA |
| | | Neg near co | 80 | 0.92 | 0.07 | 7.3 | ≤12% (%CV) | Pass | 0.07 | 7.9 | ≤15% (%CV) | Pass |
| | | Pos near co | 80 | 1.75 | 0.07 | 3.9 | ≤12% (%CV) | Pass | 0.08 | 4.8 | ≤15% (%CV) | Pass |
| | | Pos mid | 80 | 3.04 | 0.09 | 3.1 | ≤12% (%CV) | Pass | 0.12 | 3.8 | ≤15% (%CV) | Pass |
| | | Pos high | 80 | 9.27 | 0.25 | 2.6 | ≤12% (%CV) | Pass | 0.29 | 3.1 | ≤15% (%CV) | Pass |

(Continues)

**TABLE 2** (Continued)

| System: ADVIA Centaur XPT | | | | | Repeatability | | | | Within-lab precision | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Assay | Lot | Sample | *n* | Mean | SD | %CV | Acceptance criteria | Pass/fail | SD | %CV | Acceptance criteria | Pass/fail |
| HCV | 1 | Low neg | 80 | 0.08 | 0.01 | 11.3 | NA | NA | 0.03 | 40.5 | NA | NA |
| | | Neg near co | 80 | 0.62 | 0.02 | 3.2 | ≤10% (%CV) | Pass | 0.05 | 8.8 | ≤15% (%CV) | Pass |
| | | Pos near co | 80 | 1.46 | 0.05 | 3.2 | ≤10% (%CV) | Pass | 0.09 | 6.1 | ≤15% (%CV) | Pass |
| | | Pos mid | 80 | 2.73 | 0.09 | 3.2 | ≤10% (%CV) | Pass | 0.17 | 6.2 | ≤15% (%CV) | Pass |
| | | Pos high | 80 | 5.57 | 0.19 | 3.4 | ≤10% (%CV) | Pass | 0.35 | 6.3 | ≤15% (%CV) | Pass |
| | 2 | Low neg | 80 | 0.15 | 0.00 | 3.1 | NA | NA | 0.04 | 24.1 | NA | NA |
| | | Neg near co | 80 | 0.65 | 0.02 | 2.4 | ≤10% (%CV) | Pass | 0.05 | 7.8 | ≤15% (%CV) | Pass |
| | | Pos near co | 80 | 1.43 | 0.04 | 2.7 | ≤10% (%CV) | Pass | 0.07 | 4.8 | ≤15% (%CV) | Pass |
| | | Pos mid | 80 | 2.62 | 0.07 | 2.8 | ≤10% (%CV) | Pass | 0.12 | 4.6 | ≤15% (%CV) | Pass |
| | | Pos high | 80 | 5.41 | 0.16 | 2.9 | ≤10% (%CV) | Pass | 0.25 | 4.7 | ≤15% (%CV) | Pass |
| | 3 | Low neg | 80 | 0.07 | 0.00 | 4.8 | NA | NA | 0.03 | 39.2 | NA | NA |
| | | Neg near co | 80 | 0.66 | 0.02 | 2.8 | ≤10% (%CV) | Pass | 0.06 | 8.4 | ≤15% (%CV) | Pass |
| | | Pos near co | 80 | 1.54 | 0.04 | 2.3 | ≤10% (%CV) | Pass | 0.06 | 4.2 | ≤15% (%CV) | Pass |
| | | Pos mid | 80 | 2.88 | 0.08 | 2.9 | ≤10% (%CV) | Pass | 0.13 | 4.4 | ≤15% (%CV) | Pass |
| | | Pos high | 80 | 5.82 | 0.18 | 3.0 | ≤10% (%CV) | Pass | 0.36 | 6.3 | ≤15% (%CV) | Pass |
| HBcT2 | 1 | HBCT2 CN1 | 80 | 0.35 | 0.02 | 6.0 | NA | NA | 0.04 | 11.1 | NA | NA |
| | | HBCT2 CN2 | 80 | 0.88 | 0.03 | 3.9 | ≤10% (%CV) | Pass | 0.06 | 6.9 | ≤12% (%CV) | Pass |
| | | HBCT2 CP1 | 80 | 1.86 | 0.05 | 2.7 | ≤10% (%CV) | Pass | 0.12 | 6.3 | ≤12% (%CV) | Pass |
| | | HBCT2 CP2 | 80 | 3.47 | 0.13 | 3.6 | ≤10% (%CV) | Pass | 0.24 | 6.8 | ≤12% (%CV) | Pass |
| | | HBCT2 CP6 | 80 | 7.32 | 0.41 | 5.5 | ≤10% (%CV) | Pass | 0.51 | 6.9 | ≤12% (%CV) | Pass |
| | 2 | HBCT2 CN1 | 80 | 0.25 | 0.02 | 9.3 | NA | NA | 0.03 | 12.8 | NA | NA |
| | | HBCT2 CN2 | 80 | 1.00 | 0.04 | 3.9 | ≤10% (%CV) | Pass | 0.05 | 4.5 | ≤12% (%CV) | Pass |
| | | HBCT2 CP1 | 80 | 1.77 | 0.06 | 3.4 | ≤10% (%CV) | Pass | 0.08 | 4.3 | ≤12% (%CV) | Pass |
| | | HBCT2 CP2 | 80 | 3.63 | 0.11 | 3.0 | ≤10% (%CV) | Pass | 0.13 | 3.6 | ≤12% (%CV) | Pass |
| | | HBCT2 CP6 | 80 | 9.33 | 0.30 | 3.2 | ≤10% (%CV) | Pass | 0.39 | 4.1 | ≤12% (%CV) | Pass |
| | 3 | HBCT2 CN1 | 80 | 0.36 | 0.01 | 2.7 | NA | NA | 0.02 | 4.4 | NA | NA |
| | | HBCT2 CN2 | 80 | 0.91 | 0.03 | 3.2 | ≤10% (%CV) | Pass | 0.05 | 5.1 | ≤12% (%CV) | Pass |
| | | HBCT2 CP1 | 80 | 1.60 | 0.04 | 2.7 | ≤10% (%CV) | Pass | 0.08 | 5.0 | ≤12% (%CV) | Pass |
| | | HBCT2 CP2 | 80 | 3.28 | 0.11 | 3.2 | ≤10% (%CV) | Pass | 0.18 | 5.5 | ≤12% (%CV) | Pass |
| | | HBCT2 CP6 | 80 | 7.97 | 0.50 | 6.3 | ≤10% (%CV) | Pass | 0.62 | 7.8 | ≤12% (%CV) | Pass |

[†]NA = no change in clinical interpretation. An acceptance criterion of NA was allowed for negative samples with no analyte.
CHIV: ADVIA Centaur CHIV assay; Cut-off: <1.0 Index Value (Index) is considered nonreactive for p24 antigen and/or antibodies to HIV-1/HIV-2.
HBcT: ADVIA Centaur HBc Total assay; Cutoff: <0.50 Index is considered non-reactive for total antibodies to hepatitis B core antigen.
HBsAgII: ADVIA Centaur HBsAgII assay; Cutoff: <1.0 Index is considered nonreactive/negative for HBsAg.
HCV: ADVIA Centaur HCV assay; Cutoff: <0.80 Index is considered nonreactive/negative for IgG antibodies to HCV.
HBcT2: ADVIA Centaur HBc Total assay; Cutoff: < 1.0 Index is considered non-reactive for total antibodies to hepatitis B core antigen.
The samples for HBcT2 precision are pooled deceased donor serum spiked with high titer hepatitis B core positive serum.

## 3.2 | Specificity

The ADVIA Centaur CHIV, HBcT, HBsAgII, HCV, and HBcT2 assays demonstrated acceptable specificity for post-mortem specimens. Table 3 summarizes the resolved %CV specificity for each reagent lot. Although this is a relatively small sample size for specificity calculation, the results were similar for pre- and post-mortem specimens.

## 3.3 | Analytical sensitivity

Table 4 summarizes the sensitivity study using spiked samples for all reagent lots. The ADVIA Centaur CHIV, HBcT, HBsAgII, HCV, and HBcT2 assays all demonstrated acceptable sensitivity with post-mortem specimens. All sensitivity %difference results for CHIV, HBcT, HBsAgII, HCV, and HBcT2 met the acceptance criteria of ±25%. For the

**TABLE 3** Summary table for specificity using specimens from deceased and living donors

| Assay | Lot | Pre-mortem specimens | | Post-mortem specimens | | | |
|---|---|---|---|---|---|---|---|
| | | Specificity | 95% CI | Specificity | 95% CI | *p*-value | Pass/Fail |
| CHIV | 1 | 82/82 = 100.0% | (95.5%,100.0%) | 81/82 = 98.8% | (93.4%,99.8%) | 0.3158 | Pass |
| | 2 | 82/82 = 100.0% | (95.5%,100.0%) | 80/82 = 97.6% | (91.5%,99.3%) | 0.1548 | Pass |
| | 3 | 81/81 = 100.0% | (95.5%,100.0%) | 82/82 = 100.0% | (95.5%,100.0%) | 1.000 | Pass |
| HBcT [†] | 1 | 81/81 = 100.0% | (95.5%,100.0%) | 78/78 = 100.0% | (95.3%,100.0%) | 1.000 | Pass |
| | 2 | 81/81 = 100.0% | (95.5%,100.0%) | 78/78 = 100.0% | (95.3%,100.0%) | 1.000 | Pass |
| | 3 | 81/81 = 100.0% | (95.5%,100.0%) | 78/78 = 100.0% | (95.3%,100.0%) | 1.000 | Pass |
| HBsAgII[‡] | 1 | 83/83 = 100.0% | (95.6%, 100.0%) | 82/82 = 100.0% | (95.6%,100.0%) | 1.000 | Pass |
| | 2 | 83/83 = 100.0% | (95.6%, 100.0%) | 82/82 = 100.0% | (95.6%,100.0%) | 1.000 | Pass |
| | 3 | 83/83 = 100.0% | (95.6%, 100.0%) | 82/82 = 100.0% | (95.6%,100.0%) | 1.000 | Pass |
| HCV | 1 | 82/82 = 100.0% | (95.6%,100.0%) | 81/82 = 98.8% | (93.4%,99.8%) | 0.3158 | Pass |
| | 2 | 82/82 = 100.0% | (95.6%,100.0%) | 81/82 = 98.8% | (93.4%,99.8%) | 0.3158 | Pass |
| | 3 | 82/82 = 100.0% | (95.6%,100.0%) | 81/82 = 98.8% | (93.4%,99.8%) | 0.3158 | Pass |
| HBcT2[§] | 1 | 83/83 = 100.0% | (95.6%, 100.0%) | 72/74 = 97.3% | (90.7%, 99.3%) | 0.1317 | Pass |
| | 2 | 83/83 = 100.0% | (95.6%, 100.0%) | 72/74 = 97.3% | (90.7%, 99.3%) | 0.1317 | Pass |
| | 3 | 83/83 = 100.0% | (95.6%, 100.0%) | 73/74 = 98.6% | (92.7%, 99.8%) | 0.2880 | Pass |

CHIV: ADVIA Centaur CHIV assay; The Cut-off Index Value (Index) of 1.0 is used to determine whether a specimen is reactive or nonreactive for p24 antigen and/or antibodies to HIV-1/HIV-2 (i.e., $< 1.0$ Index = nonreactive/negative; $\geq 1.0$ Index = reactive/positive).
HBcT: ADVIA Centaur HBc Total assay; Samples with a calculated value of less than 0.50 Index are considered non-reactive for total antibodies to hepatitis B core antigen (but 0.5 to 0.99 Index = must repeat; $\geq 1.0$ Index = reactive/positive).
HBsAgII: ADVIA Centaur HBsAgII assay; Samples with an Index Value of less than 1.0 Index are considered nonreactive/negative for HBsAg (but $\geq 1.0$ to $\leq 50$ Index = must repeat; $> 50$ Index or > Index range = positive/reactive).
HCV: ADVIA Centaur HCV assay; Samples with a calculated value of less than 0.80 Index are considered nonreactive/negative for IgG antibodies to HCV (i.e., 0.8 Index to $< 1.00$ Index = must repeat. $\geq 1.00$ Index = reactive/positive).
HBcT2: ADVIA Centaur HBc Total assay; Cutoff: $< 1.0$ Index is considered non-reactive for total antibodies to hepatitis B core antigen.
[†] Four post-mortem specimens were TP and excluded from the calculations for the HBcT assay, resulting in 78 samples.
[‡] Lot 3 fell short of specimens for testing, so the assay was repeated in the USA on a different population (Boca Biolistics) with very similar demographics as the original study population.
[§] The HBcT2 assay was not commercially available in Australia at the time of testing, so this assay was performed in the USA.

ADVIA Centaur HBsAg Confirmatory assay, complete neutralization of initially reactive spiked pre-mortem and spiked post-mortem specimens was obtained for all samples.

## 4 | DISCUSSION

This is the first study to confirm that the precision, specificity, and sensitivity of infectious disease assays on the ADVIA Centaur system are equivalent between pre- and post-mortem specimens. The number of available tissue and cell transplants can be maximized, and the risk of infection transmission minimized through the screening of post-mortem specimens using immunoassay and nucleic acid testing. Mandatory serology tests for HIV, HBV, and HCV are the same in several countries, including the UK,[9] Australia/New Zealand,[7] the European Union,[14] and the USA.[3] Detection of an infectious disease in tissue, eye, or cell donors will generally exclude a donor.[15]

The precision study was performed according to CLSI Document EP05-A3[13] to follow the guidance used for the pre-mortem specimens in the manufacturer's instructions for use. The results showed that the previously established performance claims using pre-mortem samples were met for post-mortem specimens. Each analyte was tested for over 20 days in duplicate, in two runs per day (total of 80 results per specimen per lot per level; and 240 results per specimen for three lots per level). Instead of one spiked level reactive near the assay cutoff, as recommended in guidelines in several countries, the present study tested five different levels (ranging from non-spiked to high reactivity). Instead of using 20 individual pre-mortem and 20 post-mortem specimens, this study used serum pools from deceased donors.

In guidance documents, to obtain a labeling claim for the specificity of post-mortem specimens using an assay that is labeled for blood donor testing, it is recommended to obtain matched pairs of pre-mortem and post-mortem serum or plasma specimens for testing from each donor.[2,12] When matched pairs are not available, it is recommended to concurrently test at least 50 different post-mortem specimens from at least 50 different deceased donors and an equal number of random pre-mortem specimens using the same reagent lots.[2,12] Clinical specificity should determine if a statistically significant difference is obtained between pre-mortem and post-mortem specimens by frequency of FP results. Analytical specificity should

**TABLE 4** Summary table of sensitivity results for serum from deceased and living donors. All mean dose differences (diff) for spiked samples from deceased donors compared to spiked samples from living subjects met the acceptance criteria of ±25%

| | | Post-mortem specimens | | Pre-mortem specimens | | Acceptance (± 25%) | |
|---|---|---|---|---|---|---|---|
| Assay | Lot | Mid pos | High pos | Mid pos | High pos | % Diff - mid | % Diff - high |
| CHIV | 1 | 3.390 | 8.408 | 3.396 | 8.480 | −0.175 | −0.851 |
| | 2 | 3.527 | 8.721 | 3.500 | 8.767 | 0.793 | −0.523 |
| | 3 | 3.527 | 7.990 | 3.622 | 8.639 | −2.609 | −7.517 |
| HBcT | 1 | 5.359 | 7.653 | 5.267 | 7.743 | 1.758 | −1.162 |
| | 2 | 5.858 | 7.761 | 5.682 | 7.927 | 3.104 | −2.092 |
| | 3 | 5.672 | 7.540 | 5.574 | 7.647 | 1.754 | −1.397 |
| HBsAgII | 1 | 28.506 | 84.771 | 24.348 | 71.077 | 17.077 | 19.265 |
| | 2 | 28.163 | 88.473 | 24.299 | 75.667 | 15.899 | 16.924 |
| | 3 | 29.083 | 89.565 | 24.907 | 75.767 | 16.765 | 18.211 |
| HCV | 1 | 3.604 | 9.623 | 3.843 | 9.958 | −6.234 | −3.362 |
| | 2 | 3.518 | 9.590 | 3.664 | 10.003 | −3.984 | −4.126 |
| | 3 | 3.942 | 10.317 | 4.216 | 10.444 | −6.485 | −1.220 |
| HBcT2[†] | 1 | 2.884 | 7.851 | 2.775 | 7.639 | 3.911 | 2.776 |
| | 2 | 2.805 | 7.615 | 2.743 | 7.552 | 2.283 | 0.834 |
| | 3 | 2.886 | 7.272 | 2.823 | 7.065 | 2.235 | 2.930 |

CHIV: ADVIA Centaur CHIV assay; The Cut-off Index Value (Index) of 1.0 is used to determine whether a specimen is reactive or nonreactive for p24 antigen and/or antibodies to HIV-1/HIV-2 (i.e., < 1.0 Index = nonreactive/negative; ≥ 1.0 Index = reactive/positive).
HBcT: ADVIA Centaur HBc Total assay; Samples with a calculated value of less than 0.50 Index are considered non-reactive for total antibodies to hepatitis B core antigen (but 0.5 to 0.99 Index = must repeat; ≥ 1.0 Index = reactive/positive).
HBsAgII: ADVIA Centaur HBsAgII assay; Samples with an Index Value of less than 1.0 Index are considered nonreactive/negative for HBsAg (but ≥ 1.0 to ≤ 50 Index = must repeat; > 50 Index or > Index range = positive/reactive).
HCV: ADVIA Centaur HCV assay; Samples with a calculated value of less than 0.80 Index are considered nonreactive/negative for IgG antibodies to HCV (i.e., 0.8 Index to < 1.00 Index = must repeat; ≥ 1.00 Index = reactive/positive).
HBcT2: ADVIA Centaur HBc Total assay; Cutoff: < 1.0 Index is considered non-reactive for total antibodies to hepatitis B core antigen.
[†]Performed in the USA.

determine if a statistically significant difference is found between pre-mortem and post-mortem specimens by signal strength. Because it is difficult to obtain large numbers of matched pre-mortem and post-mortem specimens, ≥50 pre-mortem and ≥50 post-mortem unmatched specimens were tested for specificity using three reagent lots. No statistically significant difference was found between the pre-mortem and post-mortem specimens for both clinical and analytical specificity.

When matched pairs of pre-mortem and post-mortem serum or plasma specimens are not available for sensitivity studies, it is recommended to test a minimum of 50 non-reactive post-mortem specimens from 50 different deceased donors and an equal number of random pre-mortem specimens using the same reagent lots. Both types of specimens should be spiked with the infectious disease marker at a level near the assay cutoff with at least five individual positive sources.[2,12] It should be determined if a statistically significant difference exists between the spiked pre-mortem and post-mortem specimens by signal strength. Here, the sensitivity study fulfilled requirements by comparing 50 pre-mortem and 50 post-mortem specimens for three kit lots. No significant difference was found between the spiked pre-mortem and spiked post-mortem specimens. The present study demonstrated equivalent detection of an analyte in pre-mortem and post-mortem specimens and confirmed the absence of factors that might interfere with assay performance or degrade the analyte to undetectable levels. Specimens from infectious disease-free deceased donors were spiked because large numbers of specimens from infected deceased donors were not available. The study herein showed that spiked analyte was not compromised by interferents in post-mortem serum. Others, such as Kalus et al. in Germany, Kitchen et al. in the UK, and Kok et al. in Australia have also found equivalent results for infectious disease assays when comparing pre-mortem and post-mortem specimens[16–19] The Kok et al. study demonstrated that the specificity for HIV, HBV, and HCV assays on the ARCHITECT system was equivalent for 25 post-mortem and 25 pre-mortem non-spiked specimens using three different reagent lots—as was sensitivity for 25 post-mortem and 25 pre-mortem spiked specimens. Their reproducibility studies included 20 post-mortem and 20 pre-mortem specimens spiked near the cutoff in six different runs.[17] Kitchen et al. demonstrated that the performance of assays to detect infectious disease analytes (including HIV, HBV, and HCV) in 14 spiked post-mortem and pooled normal pre-mortem serum was equivalent. Each of the 14 post-mortem samples and the control normal pre-mortem serum was spiked with each of six confirmed positive samples per marker. Results of serial dilutions were equivalent for spiked post-mortem and spiked normal pre-mortem serum.[18] These

studies, like the study herein, validate the spiking method for evaluating assays on post-mortem specimens.

Other concerns included whether serological testing was valid and reliable for specimens obtained from infected deceased donors (non-spiked) as would be tested in real-life settings.[16,20,21] The issue was that infected post-mortem blood might degrade during the collection and storage process more than post-mortem specimens that were tested directly after thawing and spiking. However, Greenwald et al. compared matched pre-mortem and post-mortem results for the ability of licensed assays (Abbott, Ortho, BioRad) to detect infection and confirmed that greater than 93% of deceased donors with HIV, HBV, and HBC pre-mortem were serologically positive post-mortem. Notably, combining serology with nucleic acid testing (to cover the serological window) increased the positivity to 97%.[21] In another study by Baleriola et al., all nine pre-mortem HIV and HCV positive results were confirmed in matched post-mortem specimens using serological tests.[16] Edler et al. confirmed the pre-mortem positive status of HIV, HCV, and HBV individuals by serology testing of specimens collected up to 48 h post-mortem.[20] These results provided reassurance that serological assays could reliably detect and confirm infection in post-mortem specimens.

Millions of tissue transplants are performed each year worldwide. In Germany, in the decade up to 2018, close to 60 000 corneas, hundreds of cardiovascular tissues, and hundreds of thousands of bone preparations were transplanted.[22] In the USA alone, approximately 58 000 tissue donors provide for the 2.5 million tissue transplants performed each year.[23] Cell and Tissue transplants are important for restoring sight (corneal grafts), faulty heart function (heart valves); several diseases/conditions (hematopoietic stem cells); and for burn injuries, torn ligaments, musculoskeletal repairs, and orthopedic, spinal, dental, oral-maxillofacial, and plastic and reconstructive surgeries. Tissues, cells, and organs from one donor can help over 10 individuals; one donor potentially provides over 75–100 tissue grafts.[15,24] Unlike organs, some tissues and cells can be processed and stored for several years – benefiting multiple recipients; however, they also have the potential to infect more individuals if donors are not properly screened and tested. A US study found that the likelihood of undetected HBV, HCV, HIV, and human T-cell lymphotropic virus (HTLV) infections at the time of tissue donation (deceased donors mostly) was between about 0.1% to 1.1% and higher for tissue donors than first-time blood donors.[1] The incidence of transmission infection with tissue and cell allografts from deceased donors is unknown but believed rare and lower than the approximately 1% risk estimated for organ recipients. The lower risk with tissues and cells has been attributed to post-collection decontamination (chemical or radiation) of some products.[15,25] In addition, infection transmission may be more likely to occur and be recognized in immunocompromised organ recipients.[15] For organs, in Australia and the USA between 2008 and 2016–17, the rate of transmission of an organ donor-derived infectious disease was estimated to be 0.18%, and transmission and mortality rates were ten-fold higher for organs from deceased than living donors.[26–28] It is more challenging to quantify the risk of infection transmission by tissue and cell transplants due to difficulty in distinguishing whether the infection resulted from surgery, tissue processing, post-transplant environment, or donor transmission – and the lack of adequate surveillance, testing, tracking, reporting systems, and coordination of activities between all stakeholders. Several groups have provided recommendations for quality improvements and traceability to minimize risk.[15,24,29]

Benefits to using a well-qualified assay such as the ADVIA Centaur system include the importance of accurate detection of communicable diseases in a situation where there is a significantly different risk/benefit ratio as compared to organ transplantation.

Specifically, unlike the situation with living or organ donors, there will be no future chance to collect a second blood sample. The assay should be sensitive enough to avoid an FN result which could lead to infection of several recipients from a single donor; this could pose a higher risk for tissue and cell than organ transplantation because the number of recipients is potentially greater. An FP result would lead to discarding valuable cells and tissues that could benefit many on waiting lists.

Reports have highlighted pre-analytic procedures with the potential to affect sample quality, assay results, and risk when testing post-mortem specimens.[15,24,29] Notably, a "clotting phenomenon" has been reported where the matrix is thicker causing blockage of pipetting systems.[19] Albeit rare, this "clotting phenomenon" may "gum up" instruments causing down-time and invalid results. Here, during early testing, we observed persistent FP results caused by endogenous lipid that floated on the surface of samples following centrifugation. The lipid was drawn into the pipette tip during sample aspiration causing the tip to clog, leading to an integrity error. This problem was overcome by proactively reviewing each sample and removing the lipid layer manually before placing the tube onto the instrument. It is worth noting that floating lipid is not a unique problem with post-mortem specimens but may be observed at a higher rate in this population. We agree that post-mortem serum may be of poor quality. Fortunately, the samples purchased from Boca Biolistics were of reasonable quality; viscosity was not an issue, although some samples did show obvious signs of hemolysis and icterus. Specificity studies have an inherent limitation when using specimens from individuals whose true communicable disease status is unknown. For example, when positive results are obtained in several assays and the specimens are excluded from the specificity calculations, one cannot rule out that an interfering substance could cause an FP result in more than one assay. Here, we observed six samples that were reactive in the HBcT assay, four of which were assigned as TP based on supplemental testing. The four samples were excluded from the specificity dataset, reducing the panel size from 82 to 78 specimens. However, these four specimens were included in the specificity testing for CHIV, HBsAgII, and HCV, indicating that the reactivity seen in the HBcT assay was unlikely due to interfering substances within the post-mortem specimen. No other specimens were excluded from the study.

This study had strengths and limitations. Strengths included the large numbers of post-mortem specimens tested (74–82 specimens for specificity and 50 specimens for sensitivity). Also, precision studies were performed on five levels over 20 days. Unfortunately, donor characteristics were not available for the 83 pre-mortem specimens, except

that they were non-reactive for all analytes tested in this study. Other limitations included that hemolysis and long-term specimen stability on assay performance were not assessed; however, specificity and sensitivity results were excellent, making it unlikely that hemolysis or stability issues affected assay performance in this study.

## 5 | CONCLUSION

In conclusion, the precision, specificity, and sensitivity of the HIV, HBV, and HCV assays on the ADVIA Centaur system were equivalent for sera from deceased and living individuals. Thus, the ADVIA Centaur CHIV, HBcT, HBsAgII, and HCV assays are acceptable for use in routine testing of sera collected from deceased donors within 24 h after cessation of the heartbeat.

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### CONFLICT OF INTEREST

Theodore B. Wright, Sai Patibandla, Renee Walsh, Rachel Fonstad, Matthew Gee, Vera Bitcon, JB, Julie Hopper, PD, Scott Read are full-time employees of Siemens Healthcare Diagnostics Inc. Susie J. Braniff and Susan Best were employees of the National Serology Reference Laboratory (NRL), Victoria, Australia.

### AUTHOR CONTRIBUTIONS

Theodore B. Wright contributed to the design of the study, interpretation of results, presentation of results, and contributed reagents. Sai Patibandla contributed to the study design, interpretation of results, and contributed reagents. Renee Walsh contributed to interpretation. Rachel Fonstad contributed to data and statistical analysis. Matthew Gee contributed to interpretation. Vera Bitcon contributed to interpretation, study concept, and contributed reagents. Julie Hopper contributed to interpretation. Susie J. Braniff and Susan Best contributed important specimens and to interpretation. Scott Read contributed to performing research study and interpretation. All authors contributed to the draft manuscript and approved the final manuscript.

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