

**VACUETTE**<sup>®</sup> Serum Clot Activator tubes, demonstrating that these proteins were not adsorbed onto the plastic walls of the tubes and interfering substances were not leached from the walls of the tubes.<sup>4,5</sup>

#### References

1. Greiner Bio-One. Evacuated Blood Collection System For In Vitro Diagnostic Use. Product Insert. Monroe, NC, July 2005.
2. FDA Center for Biologics Evaluation and Research Guidance Document. Recommended Methods for Anti-Human Globulin Evaluation. March 1992.
3. Cancelas-Perez, Jose A. MD. Hoxworth Blood Center Final Report. Greiner Vacuette Evacuated Blood Collection Tubes. Immunohematology Blood Bank Studies. Cincinnati, Ohio. March 29, 2005.
4. Greiner Bio-One 510(k) Submission. Premarket Notification for Greiner **VACUETTE**<sup>®</sup> No Additive Tube and **VACUETTE**<sup>®</sup> Clot Activator Tube – For Use in Immunohematology Testing. Monroe, NC. March 18, 2005.
5. Gruber, H. Greiner Bio-One. Product Manual. Kremsmunster, Austria. July 2002.

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# Greiner Bio-One **VACUETTE**<sup>®</sup> No Additive and Serum Clot Activator Blood Collection Tubes Evaluation for Immunohematology Summary

#### Device Names

Greiner Bio-One **VACUETTE**<sup>®</sup> Serum Clot Activator, 6.0mL, 13x100mm tube, Product Listing #456092

Greiner Bio-One, **VACUETTE**<sup>®</sup> No Additive, 6.0mL, 13x100mm tube, Product Listing #456001

Greiner Bio-One **VACUETTE**<sup>®</sup> Serum Clot Activator, 3.0mL, 13x75mm tube, Product Listing #454095

Greiner Bio-One **VACUETTE**<sup>®</sup> No Additive, 3.0mL, 13x75mm tube, Product Listing #454241

#### Comparator Devices

Becton Dickinson Vacutainer™ Glass, No Additive, Non-Coated Interior, 7.0mL, 13x100mm tube, Product Listing #369626

Becton Dickinson, Vacutainer™ Glass, No Additive, Non-Siliconized, 7.0mL, 13x100mm tube, Product Listing #366442

Becton Dickinson, Vacutainer™ Glass, No Additive, Interior, 3.0mL, 10.25x64mm tube, Product Listing #366397

#### Intended Use

The Greiner Bio-One **VACUETTE**<sup>®</sup> No Additive tubes and Greiner Bio-One **VACUETTE**<sup>®</sup> Serum Clot Activator tubes are made of plastic and are used for the collection of venous blood, which upon centrifugation, separates serum from the clotted cells. The Greiner Bio-One **VACUETTE**<sup>®</sup> Serum Clot Activator tubes are coated with micronized silica particles which activate clotting when the tubes are gently inverted.<sup>1</sup>

#### Specimen Collection

Blood specimens were obtained using each site's standard phlebotomy techniques referencing Standard Operating Procedures and OSHA's safety requirements for blood collection. The order of draw was randomized.

Three tubes were drawn from each donor. At Donor Center #1, one Greiner Bio-One **VACUETTE**<sup>®</sup> No Additive, 6.0mL, 13x100mm, one Greiner Bio-One **VACUETTE**<sup>®</sup> Serum Clot Activator, 6.0mL, 13x100mm and one Becton Dickinson Vacutainer™ Glass, No Additive, Non-Coated Interior, 7.0mL, 13x100mm tubes were drawn. At Donor

Center #2, one Greiner Bio-One **VACUETTE**<sup>®</sup> No Additive, 6.0mL, 13x100mm, one Greiner Bio-One **VACUETTE**<sup>®</sup> Serum Clot Activator, 6.0mL, 13x100mm and one Becton Dickinson Vacutainer™ Glass, No Additive, Non-Siliconized, 7.0mL, 13x100mm tubes were drawn. At the University Hospital, in order to minimize the amount of blood drawn from patients, this study was divided into two parts. For Part I, one Greiner **VACUETTE**<sup>®</sup> Serum Clot Activator, 3.0mL, 13x75mm and one Becton Dickinson Vacutainer™ Glass, No Additive, Non-Siliconized Interior, 3.0mL, 10.25x64mm tubes were drawn. For Part II, one Greiner Bio-One **VACUETTE**<sup>®</sup> No Additive, 3.0mL, 13x75mm and one Becton Dickinson Vacutainer™ Glass, No Additive, Non-Siliconized Interior, 3.0mL, 10.25x64mm tubes were drawn.

#### A. Donor Center - Site #1:

- 1) 50 prospectively collected donors
- 2) 15 selected individuals with antibodies
- 3) Subset of antibody positive individuals (half draw) [n=10]
- 4) Subset of antibody positive individuals (full and half draw) for repeat testing at Day 14 [n=10]
- 5) Subset of prospectively collected donors (full draw and half draw) for antigen phenotyping (13 antigens) [n=10]
- 6) Subset of prospectively collected donors (full draw) for repeat antigen phenotyping at Day 14 [n=10]
- 7) DAT positive individuals tested at Days 0, 7, and 14 [n=5]

#### B. Donor Center - Site #2:

The following donors were drawn:

- 1) 50 prospectively collected donors;
- 2) 15 selected individuals with antibodies
- 3) Subset of prospectively collected donors (full draw) for antigen testing [n=11] apparently healthy donors

#### C. University Hospital - Site #3:

56 (Part I, Clot Activator) and - 50 (Part II, No Additive) patients of various disease states whose physician ordered a blood transfusion:

- 1) Liver
- 2) Cardiovascular
- 3) Hematology (Leukemia, Lymphoma, Multiple Myeloma, Sickle Cell Disease)
- 4) Gastrointestinal
- 5) Urogenital
- 6) Neurology
- 7) Pulmonary
- 8) ENT (Ear, Nose, Throat)
- 9) Renal
- 10) Breast (Cancer of the Breast, Mastectomy)

### Handling Techniques

The tubes were gently mixed using ten complete inversions immediately following blood collection. Tubes were centrifuged using the laboratory's standard procedure, to separate cellular elements completely from the serum.

### Study Design

Studies were conducted at two commercial blood banks and one university hospital blood bank to evaluate the use of the Greiner Bio-One **VACUETTE**® No Additive and the Greiner Bio-One **VACUETTE**® Serum Clot Activator tubes in Immunohematology testing. IRB approval was obtained on the submitted protocol. Informed Consent was signed by each participant. The order of tube draw was randomized. The study design was based on recommendations made by reviewers from the FDA Center for Biologics Evaluation and Research, Division of Blood Applications (CBER).<sup>2</sup>

### Instrumentation and Tests

#### A. Donor Center - Site #1:

- 1) Manual Method: ABO, Rh, DAT, Antibody Screening and Identification, Antigen Phenotyping
- 2) Sample Stability Study/Delay in Testing:
  - a) Antibody Positive Samples: ABO, Rh, DAT, Antibody Screening and Identification using full and half draw/half-evacuated tubes
  - b) Antigen Phenotyping Samples: Antigen Phenotyping using full draw tubes

#### B. Donor Center - Site #2:

- 1) Manual Method: ABO, Rh, DAT, Antigen Phenotyping, Antibody Screening and Identification
- 2) Ortho ID-Micro Typing System™ (ID-MTS) Gel Test™: Antibody Screening and Identification

#### C. University Hospital - Site #3:

- 1) Manual Method: ABO, Rh, DAT, Antibody Screening and Identification
- 2) Standard LISS Tube Method: Antibody Screening and Identification

### Discussion

#### ABO/Rh Testing

ABO/Rh typing was performed on matching tubes of blood from 98 apparently healthy blood donors, 15 known antibody positive blood donors and 106 hospitalized patients. The testing was performed manually. Concordant results were obtained with the Greiner Bio-One **VACUETTE**® No Additive, the Greiner Bio-One **VACUETTE**® Serum Clot Activator and the BD Vacutainer™ Glass, No Additive, Non-Coated and Non-Siliconized Interior tubes.

#### Antigen Phenotyping

Antigen phenotyping was performed on matching tubes of blood from 21 apparently healthy blood donors. The samples were screened for the most commonly detected antigens of the MNS blood group system (such as S and s antigens) and low incidence antigens in other blood group systems (such as C, E, c, e, K, FY<sup>a</sup>, FY<sup>b</sup>, JK<sup>a</sup>, JK<sup>b</sup>).

The distribution of results is summarized in Table #1. Concordant results were obtained with the Greiner Bio-One **VACUETTE**® No Additive, the Greiner Bio-One **VACUETTE**® Serum Clot Activator tube and the BD Vacutainer™ Glass, No Additive, Non-Coated Interior and Non-Siliconized Interior tubes.

Table #1		
	Donor Center - Site #1	Donor Center - Site #2
	(#Pos/#Neg)	(#Pos/#Neg)
C	5/5	7/4
E	3/7	1/10
c	9/1	9/2
e	10/0	11/0
K	2/8	0/11
FY <sup>a</sup>	8/2	8/3
FY <sup>b</sup>	7/3	7/4
FY <sup>b</sup>	7/3	9/2
JK <sup>a</sup>	8/2	7/4
JK <sup>b</sup>	6/4	5/6
S	10/0	11/0
s	10/0	NT
M	8/2	NT
N	5/5	7/4

\* NT = Not Tested

At both sites, grading of the reactivity was performed, using a scale of 1+ to 4+. All antigen results for the Greiner tubes were within a 1+ grade of the BD tube. This variation is within the expected reproducibility of a subjective grading system.

### Antibody Screening and Identification

#### Full Draw Tube

Antibody screening was performed on healthy blood donors, known antibody positive blood donors and hospitalized patients using the Greiner Bio-One **VACUETTE**® No Additive tube, the Greiner Bio-One **VACUETTE**® Serum Clot Activator tube and the BD Vacutainer™ Glass, No Additive, Non-Coated Interior and Non-Siliconized Interior tubes at full draw. At Site #1, testing was performed using a manual tube method. Site #2 used two methods, a standard gel test and a standard tube test at immediate spin and 37°C.<sup>3</sup> All antibody screening positive samples were followed up with antibody identification testing.

Concordant results were obtained with the Greiner Bio-One **VACUETTE**® No Additive, the Greiner Bio-One **VACUETTE**® Serum Clot Activator tube and the BD Vacutainer™ Glass, No Additive, Non-Coated Interior and Non-Siliconized Interior tubes. In some of the comparisons, there was a 1+ difference, but none of these results demonstrated a change to a negative reading. This variation is within the expected reproducibility of a subjective grading system.

#### Half-Draw Tube

At Site #1, ABO/Rh typing, antibody screening and antibody identification were performed on a subset of 10 of the known antibody positive blood donors using the Greiner Bio-One **VACUETTE**® No Additive and the Greiner Bio-One **VACUETTE**® Serum Clot Activator full and half draw tubes and the BD Vacutainer™ Glass, No Additive, Non-Coated Interior tubes at full draw. The testing was performed using a manual system according to the established procedure.

Concordant results were obtained with the Greiner Bio-One **VACUETTE**® No Additive and Greiner Bio-One Serum Clot Activator full and half draw tubes and the BD Vacutainer™ Glass, No Additive, Non-Coated Interior tubes full draw tubes. In some of the samples, there was a 1+ difference in the results. This variation is within the expected reproducibility of a subjective grading system.

#### Delay in Testing

At Site #1, the 10 antigen phenotyping samples and 10 of the known antibody positive blood donor samples (full and half-draw tubes) were stored at 2-8°C following initial

testing. Testing was repeated at 14 days after collection. The antigen phenotyping samples were only repeated for antigen phenotyping testing. The known antibody positive blood donor samples were repeated for ABO/Rh typing, antibody screening and identification.

Concordant results were obtained with the Greiner Bio-One **VACUETTE**® No Additive and the Greiner Bio-One **VACUETTE**® Serum Clot Activator full and half draw tubes and the BD Vacutainer™ Glass, No Additive, Non-Coated Interior at Day 14. In some of the samples, there was a 1+ difference in the results. This variation is within the expected reproducibility of a subjective grading system.

### DAT

Direct Antibody Testing (DAT) was performed on the 98 healthy blood donors, the 15 known antibody positive blood donors and the 5 known DAT positive individuals (Site #2) and the 106 hospitalized patients using the Greiner Bio-One **VACUETTE**® No Additive, the Greiner Bio-One **VACUETTE**® Serum Clot Activator and the BD Vacutainer™ Glass, No Additive, Non-Coated Interior and Non-Siliconized Interior tubes. There were no DAT positive results among the 98 blood donors and 15 known antibody positive blood donors. Four of the 5 known DAT positive individuals were DAT positive in this study. One individual was DAT inconclusive with a 2+ Saline Control. Concordant results were obtained with the Greiner Bio-One **VACUETTE**® No Additive, the Greiner Bio-One **VACUETTE**® Serum Clot Activator and the BD Vacutainer™ Non-Coated Interior tubes.

In addition, the DAT testing on the known DAT positive samples was repeated on Days 7 and 14. Concordant results were obtained with the Greiner Bio-One **VACUETTE**® No Additive, the Greiner Bio-One **VACUETTE**® Serum Clot Activator and the BD Vacutainer™ Glass, Non-Coated Interior tubes on Days 0, 7, and 14. In some of the samples, there was a 1+ difference in the results. This variation is within the expected reproducibility of a subjective grading system.

### Conclusion

The Greiner Bio-One **VACUETTE**® No Additive and Greiner Bio-One **VACUETTE**®, Serum Clot Activator tubes (full and half draw/half-evacuated) demonstrated substantial equivalence to the Becton Dickinson Vacutainer™ Glass, Non-Coated Interior and Non-Siliconized Interior tubes with various standard assays using donor and recipient populations. Antigen and antibody identification did not change over time when samples were stored in the Greiner Bio-One **VACUETTE**® No Additive and Greiner Bio-One