WHITE PAPER

TECHNICAL NOTES & APPLICATIONS FOR LABORATORY WORK

EVALUATION OF VACUETTE® CAT SERUM FAST SEPARATOR BLOOD COLLECTION TUBE FOR ROUTINE CHEMISTRY ANALYTES **IN COMPARISON TO VACUTAINER® RST TUBE**

CONTENT

1/ BACKGROUND

Greiner-Bio-One, Austria has been selling plastic evacuated tubes (VACUETTE®) for venous blood collection since 1986. VACUETTE® CAT Serum Fast Separator blood collection tubes contain thrombin in addition to the blood clotting activator to further accelerate the clotting process.

Due to the rapid clotting process within 5 minutes after blood collection and the following centrifugation, the VACUETTE® CAT Serum Fast Separator blood collection tubes enable faster turnaround times similar to plasma tubes. According to the available study results, the tubes are suitable for the usage for routine chemistry analyses. Patients who are on heparin or other thrombin inhibitor therapy were not included in this study design[1].

The VACUETTE® CAT Serum Fast tube is offered as a gel separator tube. The gel has a specific gravity, forms a stable barrier between the blood cells and the serum during centrifugation and provides stability for most analytes up to 48h when measured out of the primary tube stored at room temperature (RT) for 24h and following at 4-8°C in the refrigerator up to 48h.

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2/ STUDY OBJECTIVE

The study has been carried out to demonstrate method comparison of modified VACUETTE® CAT Serum Fast Separator blood collection tubes to VACUTAINER® RST Blood Collection tubes when centrifuged at 1800g for 10 min for routine chemistry analysis. The objective of the study was to show representative biochemical analytes in VACUETTE® CAT Serum Fast Separator blood collection tubes when centrifuged at 1800g/10 min as well as at 3000g/5 min.

3/ STUDY DESIGN AND PROCEDURE

Venous blood was collected from 20 healthy donors aged 18-64 years by using a VACUETTE® Disposable Tourniquet (Item n° 840053), a VACUETTE® EVOPROTECT SAFETY Blood Collection Set + Holder (Item n° 450120), and a VACUETTE® No Additive tube as discard tube (Item n° 454001) into the following tubes:

Sample	Tube description	Item N°	Volume [ml]	Centrifugation
A	VACUTAINER® RST Tube	368774	5	1800g / 10 min / 20°C
B	VACUETTE® CAT Serum Fast Separator Tube	456309	5	1800g / 10 min / 20°C
C	VACUETTE® CAT Serum Fast Separator Tube	456309	5	3000g / 5 min / 20°C

One tube of each sample was drawn from each donor. All samples were gently inverted 5 times. After a minimum of 5 min. clotting time of the whole blood sample in an upright position, all samples were centrifuged within max. 2h according to the centrifugation setting in the table above at 20°C (centrifuge: Hettich Rotanta 460R for Sample A and B; Hettich Rotanta 420R for Sample C).

After centrifugation, all samples were visually inspected if there were any floating clots in the serum. Initial analysis was done after centrifugation on an AU680 and DxI800 from Beckman Coulter. Free hemoglobin was determined according to Harboe for samples centrifuged at 1800g for 10min.

4/ METHOD COMPARISON ANALYTES ON BECKMAN COULTER AU680 AND DXI800

Parameter	Abbreviation	Acceptance criteria CAL: [2]Rili-BÄK/ [3]CLIA / [4]BV
Alanine Transaminase	ALT	11.50[2]
Albumin	ALB	8.00[3]
Alkaline Phosphatase	ALP	11.00[2]
Complement 3	C3	8.40[4]
Calcium	Ca	6.00[2]
Cholesterol	CHOL	7.00[2]
Cortisol	Cort	16.00[2]
Creatine Kinase	CK	11.00[2]
Chloride	Cl	4.50[2]
C-reactive Protein	CRP	13.50[2]
Creatinine	Crea	10.00[3]
Estradiol	E2	22.00[2]
Iron	Fe	20.00[2]
Folic Acid	FOL	25.00[2]
Follicle stimulation hormone	hFSH	18.00[3]
Free Triiodothyronine	fT3	13.00[2]
Gamma Glutamyltransferase	GGT	11.50[2]
Glucose	Gluc	8.00[3]
High Density Lipoprotein	HDL	13.00[2]
Immunglobuline G	IgG	10.00[2]
Inorganic Phoshate	IP	9.00[2]
Lactate-Dehydrogenase	LDH	9.00[2]
Magnesium	Mg	15.00[3]

Parameter	Abbreviation	Acceptance criteria CAL: [2]Rili-BÄK/ [3]CLIA / [4]BV
Potassium	K	4.50[2]
Sodium	Na	3.00[2]
Thyroid-stimulating hormone	TSH	13.50[2]
Total Bilirubin	TBil	20.00[3]
Total Protein	TP	6.00[2]
Triglyceride	TG	9.00[2]
Urea	Urea	9.00[3]
Uric Acid	UA	7.00[2]
Cobalamine (Vitamin B_{12})	VitB_{12}	25.00[3]
Lipemic Icteric Haemolysis Index	LIH	N.A.

Statistics were performed using GLIMS (Software Laboratory information system for tracking/identification of samples, Version 1.3.0) for method comparison.

Acceptance criteria for method comparison (bias estimations between sample A and B as well as between sample B and C): the overall mean estimated bias including 95% Confidence Interval (CI) for each parameter was evaluated with respect to the clinical acceptance limit (CAL). Clinical evaluation was based on the allowed recommendation by Rili-BÄK[2] guideline. If no acceptance criteria are listed in Rili-BÄK[2], CLIA[3] or BV[4] guidelines were used.

5/ RESULTS

5.1/ CLOTTING TIME

Sample	Time [sec]			
	60	120	180	240
	Distribution clotting time [%]			
A	10	65	15	0
B	15	75	10	0
C	15	55	25	5

5.2/ DETERMINATION OF FREE HEMOGLOBIN

Sample	Median fHb
A	3.5 mg/dl
B	2.3 mg/dl

5.3/ METHOD COMPARISON – INITIAL MEASUREMENT

Analyte	Sample	Centrifugation	Mean	SD
ALB [g/l]	A	1800g/ 10 min	43.34	2.10
	B	1800g/ 10 min	43.42	2.36
	C	3000g/ 5 min	43.47	2.26
ALP [U/l]	A	1800g/ 10 min	57.83	13.65
	B	1800g/ 10 min	57.75	13.20
	C	3000g/ 5 min	57.85	13.55
ALT [U/l]	A	1800g/ 10 min	23.98	16.65
	B	1800g/ 10 min	24.20	16.38
	C	3000g/ 5 min	24.35	16.83
C3 [mg/dl]	A	1800g/ 10 min	117.65	16.28
	B	1800g/ 10 min	117.70	15.10
	C	3000g/ 5 min	117.75	14.65
Ca [mmol/l]	A	1800g/ 10 min	2.30	0.084
	B	1800g/ 10 min	2.29	0.094
	C	3000g/ 5 min	2.31	0.079
CHOL [mg/dl]	A	1800g/ 10 min	203.95	40.53
	B	1800g/ 10 min	204.65	39.81
	C	3000g/ 5 min	204.97	40.29

Analyte	Sample	Centrifugation	Mean	SD
CK [U/l]	A	1800g/ 10 min	123.45	67.81
	B	1800g/ 10 min	123.47	67.72
	C	3000g/ 5 min	123.62	68.57
Cl [mmol/l]	A	1800g/ 10 min	104.40	1.98
	B	1800g/ 10 min	104.38	2.08
	C	3000g/ 5 min	104.62	2.33
Cort [mg/dl]	A	1800g/ 10 min	8.43	3.06
	B	1800g/ 10 min	8.49	2.95
	C	3000g/ 5 min	8.37	3.00
CRP [mg/l]	A	1800g/ 10 min	2.27	5.28
	B	1800g/ 10 min	2.20	4.96
	C	3000g/ 5 min	2.24	5.12
Fe [µmol/l]	A	1800g/ 10 min	16.61	8.38
	B	1800g/ 10 min	16.69	8.48
	C	3000g/ 5 min	16.69	8.57
FOL [ng/ml]	A	1800g/ 10 min	7.91	3.04
	B	1800g/ 10 min	7.68	3.20
	C	3000g/ 5 min	7.72	3.14
fT3 [pg/ml]	A	1800g/ 10 min	3.21	0.31
	B	1800g/ 10 min	3.22	0.30
	C	3000g/ 5 min	3.25	0.30
GGT [U/l]	A	1800g/ 10 min	23.45	22.08
	B	1800g/ 10 min	23.48	21.77
	C	3000g/ 5 min	23.62	22.29

Analyte	Sample	Centrifugation	Mean	SD
Gluc [mg/dl]	A	1800g/ 10 min	96.38	22.20
	B	1800g/ 10 min	95.72	21.79
	C	3000g/ 5 min	96.97	21.85
HDL [mg/dl]	A	1800g/ 10 min	59.91	10.77
	B	1800g/ 10 min	60.10	11.07
	C	3000g/ 5 min	60.50	11.51
hFSH [mIU/ml]	A	1800g/ 10 min	17.60	23.49
	B	1800g/ 10 min	18.07	24.00
	C	3000g/ 5 min	17.63	23.15
IgG [mg/dl]	A	1800g/ 10 min	1027.28	224.25
	B	1800g/ 10 min	1031.67	225.81
	C	3000g/ 5 min	1028.92	217.54
IP [mmol/l]	A	1800g/ 10 min	1.04	0.15
	B	1800g/ 10 min	1.04	0.15
	C	3000g/ 5 min	1.04	0.15
K [mmol/l]	A	1800g/ 10 min	4.00	0.14
	B	1800g/ 10 min	4.00	0.15
	C	3000g/ 5 min	4.00	0.15
Crea [mg/dl]	A	1800g/ 10 min	0.84	0.14
	B	1800g/ 10 min	0.83	0.13
	C	3000g/ 5 min	0.84	0.13
LDH [U/l]	A	1800g/ 10 min	152.12	25.27
	B	1800g/ 10 min	152.95	24.16
	C	3000g/ 5 min	155.82	24.86

Analyte	Sample	Centrifugation	Mean	SD
Mg [mmol/l]	A	1800g/ 10 min	0.80	0.057
	B	1800g/ 10 min	0.81	0.058
	C	3000g/ 5 min	0.81	0.056
Na [mmol/l]	A	1800g/ 10 min	138.20	1.78
	B	1800g/ 10 min	138.35	1.82
	C	3000g/ 5 min	138.50	1.62
E2 [pg/ml]	A	1800g/ 10 min	81.65	98.94
	B	1800g/ 10 min	82.45	100.11
	C	3000g/ 5 min	83.70	106.57
TBili [mg/dl]	A	1800g/ 10 min	0.72	0.34
	B	1800g/ 10 min	0.73	0.34
	C	3000g/ 5 min	0.73	0.34
TG [mg/dl]	A	1800g/ 10 min	114.75	82.53
	B	1800g/ 10 min	114.35	82.07
	C	3000g/ 5 min	114.15	81.45
TP [g/l]	A	1800g/ 10 min	68.31	3.34
	B	1800g/ 10 min	69.00	3.17
	C	3000g/ 5 min	69.24	3.23
TSH [µIU/ml]	A	1800g/ 10 min	1.53	0.73
	B	1800g/ 10 min	1.53	0.74
	C	3000g/ 5 min	1.54	0.74
UA [mg/dl]	A	1800g/ 10 min	5.35	1.25
	B	1800g/ 10 min	5.37	1.24
	C	3000g/ 5 min	5.36	1.21

Analyte	Sample	Centrifugation	Mean	SD
Urea [mg/dl]	A	1800g/ 10 min	30.16	8.59
	B	1800g/ 10 min	30.15	8.58
	C	3000g/ 5 min	30.20	8.65
Vit B_{12} [pg/ml]	A	1800g/ 10 min	271.65	88.14
	B	1800g/ 10 min	271.68	86.36
	C	3000g/ 5 min	272.68	90.29

MEASUREMENT OF LIH:

LIH was negative in all samples for icterus and hemolysis, slightly positive in two samples for lipemia.

BIAS METHOD COMPARISON

(SAMPLE A TO B AND SAMPLE B TO C)

Analyt	Bias [%] Sample A to B (1800g/10 min)	Bias [%] Sample B (1800g/10 min) to C (3000g /5min)
	Initial time point [0h]	Initial time point [0h]
ALB	1.27	1.53
ALP	1.72	2.56
ALT	2.59	2.07
C3	1.41	1.79
Ca	1.02	1.22
CHOL	1.30	1.86
CK	1.61	2.54
Cl	0.46	0.74
Cort	4.31	3.37
CRP	2.02	2.54
Fe	1.67	2.26
FOL	6.88	5.25
fT3	2.89	4.62
GGT	1.44	4.10
Gluc	2.12	1.46
HDL	1.78	2.20

Analyt	Bias [%] Sample A to B (1800g/10 min)	Bias [%] Sample B (1800g/10 min) to C (3000g /5min)
hFSH	3.73	3.71
IgG	1.47	1.64
IP	1.01	1.49
K	1.41	1.47
Crea	2.17	1.66
LDH	2.60	3.03
Mg	1.14	1.28
Na	0.36	0.43
E2	13.62	14.03
TBili	1.71	2.28
TG	1.67	2.32
TP	1.63	2.56
TSH	4.55	2.64
UA	0.60	0.54
Urea	1.02	1.03
$VitB_{12}$	3.64	4.21

6/ SUMMARY OF RESULTS - INITIAL MEASUREMENT

For all samples, the clotting time was below 5 minutes.

CENTRIFUGATION AT 1800G FOR 10 MIN:

At initial time point, analytical testing demonstrated that comparing the modified **VACUETTE® CAT Serum Fast Sep Clot Activator tube** (Sample B) with BD **Vacutainer® RST Rapid Serum tube** (Sample A) shows clinically equivalent results for the following 32 parameters:

Comparison Sample A to B: **32 parameters** (of 32 tested) – (ALB, ALP, ALT, Ca, CHOL, CK, Cl, C3, Cort, CRP, E2, Fe, FOL, fT3, GGT, Gluc, hFSH, HDL, IGG, IP, K, Crea, LDH, Mg, Na, TBili, TG, TP, TSH, UA, Urea, $VitB_{12}$).

CENTRIFUGATION AT 3000G FOR 5 MIN:

At initial time point, analytical testing demonstrated that comparing the modified **VACUETTE® CAT Serum Fast Sep Clot Activator tube** (Sample B, centrifuged at 1800g/10 min) with **VACUETTE® CAT Serum Fast Sep Clot Activator tube** (Sample C, centrifuged at 3000g/5 min) shows clinically equivalent results for the following 32 parameters:

Comparison Sample B to C: **32 parameters** (of 32 tested) – (ALB, ALP, ALT, Ca, CHOL, CK, Cl, C3, Cort, CRP, E2, Fe, FOL, fT3, GGT, Gluc, hFSH, HDL, IGG, IP, K, Crea, LDH, Mg, Na, TBil, TG, TP, TSH, UA, Urea, $VitB_{12}$).

7/ CONCLUSION

The substantially equivalent clinical performance of the modified VACUETTE® CAT Serum Fast Separator blood collection tube in comparison to the VACUTAINER® RST blood collection tube has been demonstrated for routine biochemical analytes on a Beckman Coulter analyzer at initial time for donors who are not on any anticoagulant therapy.

By providing a clear serum after centrifugation, the utilization of the modified VACUETTE® CAT Serum Fast Separator tube enables a faster turnaround time in the laboratory due to the rapid clotting process minimizing the cell lysis in the tube within 5 minutes on the basis of the thrombin additive. Systematic differences to blood collection tubes without a clotting accelerator such as thrombin were found in studies and discussed with regard to the benefit in emergency situations but need to be taken in consideration by clinicians [5/6/7]. One study investigated the risk of hyperkalaemia in a thrombin-containing tube by measuring potassium values as well as LDH activity [8]. Another study presented stability data for a routine chemistry profile up to 4 days apart from bicarbonate, electrolytes and albumin [9].

8/ REFERENCES

[1] IFU Evacuated Blood Collection System GBO. 980200_Rev23_06_2020

[2] Rili-BÄK: Richtlinie der Bundesärztekammer zur Qualitätssicherung laboratoriumsmedizinischer Untersuchungen, https://www.bundesaerztekammer.de/aerzte/qualitaetssicherung/richtlinien-leitlinien-empfehlungen-stellungnahmen/richtlinien-leitlinien-empfehlungen-zurqualitaetssicherung/labor/ [14-FEB-2021; 14:31:00 UTC]

[3] CLIA: CLIA: Clinical Laboratory Improvement Amendments (CLIA) https://www.westgard.com/2019-clia-changes.htm [24-JUN-2022]

[4] BV: 2004 update of the Spanish Society of Clinical Chemistry and Molecular Pathology (SEQC) table of Desirable Quality Specifications based on Biological Variation

[5] S.J. Steindel, Evaluation of a Thrombin Containing Blood Collection Tube. Clin. Chem., Vol. 26, 1, (1980)

[6] M. Kojiancic, J. Cargonja, A.Delic-Knezevic. Evaluation of the BD Vacutainer RST blood collection tube for routine chemistry analytes: clinical significances of differences and stability study Biochemica Medica 2014; 24: 368-75

[7] Koch et al, BD rapid serum tubes reduce false positive plasma troponin T results on the Roche Cobas e411 analyzer. Clin Biochem 2012; 45: 842-44

[8] Huyghe T et al. Studies on the use of BD Vacutainer SSTII and RST in general practice: investigation of artefactual hyperkalemia. Ann Clin Biochem 2014; 51: 30-37

[9] W.-Y. Ng, C-P. Yeo, Thrombin-Accelerated Quick Clotting Serum Tubes: An Evaluation with 22 Common Biochemical Analytes. Advances in Hematology (Volume 2013), Advances in Hematology, Article ID 769479 http://dx.doi.org/10.1155/2013/769479

PROVIDED A CLEAR SERUM AFTER CENTRIFUGATION, THE UTILIZATION OF THE MODIFIED VACUETTE® CAT SERUM FAST SEPARATOR TUBE ENABLES A FASTER TURNAROUND TIME IN THE LABORATORY DUE TO THE RAPID CLOTTING PROCESS, MINIMIZING THE CELL LYSIS IN THE TUBE WITHIN 5 MINUTES ON THE BASIS OF THE THROMBIN ADDITIVE.

Systematic differences to blood collection tubes without a clotting accelerator such as thrombin were found in studies and discussed with regard to the benefit in emergency situations but need to be taken in consideration by clinicians.

PRODUCT & ORDERING INFORMATION

- **Only 5 minutes[2] waiting time before transport.**
- **Reduced turnaround time.**
- **Faster results.**
- **Faster diagnosis.**

Time is of the essence when it comes to accurate and fast test results for treating patients. Fast coagulation following blood collection allows crucial minutes to be saved.

Heparinized plasma is often used as an emergency tube as there is no need to wait for coagulation. Serum is sometimes indispensable in emergency departments and this is precisely where VACUETTE® CAT Serum Fast Tubes can save enormous amounts of time.[1]

The VACUETTE® CAT Serum Fast tube combines the speed of a plasma tube with the properties of serum. It allows coagulation in the whole blood sample to be completed in just 5 minutes,[2] thus considerably shortening the preanalytical process. This means targeted treatment can be initiated quicker. With a reduced centrifugation time of 5 minutes[2], the time from collection to analysis is 10 minutes instead of 35 minutes[3]. This makes it easy to effectively reduce turnaround time (TAT) by 25 minutes per sample.[1]

VACUETTE® CAT Serum Fast Separator Tube

Item No.	Nominal volume	Cap colour	Ring colour	Thread type	Tube size	Label	Barcode	Inner / Outer [Qty.]
454592	3.5 ml	orange	yellow	PREMIUM	13 x 75	Paper	no	50 / 1,200
454593	3.5 ml	orange	yellow	non-ridged	13 x 75	Paper	no	50 / 1,200
456309	5 ml	orange	yellow	PREMIUM	13 x 100	Paper	no	50 / 1,200
456313	5 ml	orange	yellow	non-ridged	13 x 100	Paper	no	50 / 1,200
486509	5 ml	orange	yellow	PREMIUM	13 x 100	Paper	yes	50 / 1,200

References and information:

1 Use of anticoagulants in diagnostic laboratory investigations. World Health Organization. WHO/DIL/LAB/99.1 Rev.2, 2002.

2 Serum Fast tubes are not intended for patients on thrombin inhibitor therapy or fibrinogen deficiency.

3 Depending on centrifugation conditions

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