

# Evaluation of VACUETTE<sup>®</sup> Serum Gel tubes for Therapeutic Drug Monitoring (TDM) in Serum

## **Background:**

Greiner-Bio-One, Austria has been selling plastic evacuated tubes (VACUETTE<sup>®</sup>) for venous blood collection since 1986.

VACUETTE<sup>®</sup> Gel Tubes incorporate an inert gel material into the blood collection tube. These gels have a controlled viscosity and a specific gravity intermediate to the serum and clot. During centrifugation, the gel material forms an impermeable barrier between the serum and clot.

Gel Z has been in development since 2001 and has the same components as the last gel type (Gel P3), the difference being the production process, which has been optimised. The gel might be slightly more yellow in colour however provides better performance than the last gel type as well as providing the advantage of a more stable barrier, which is particularly beneficial during transport.

Preanalytical handling remains the same and does not require any changes (i.e. centrifugation conditions, storage, transport, etc).

## **Study Objective:**

The aim was to study the stability of a variety of commonly monitored drugs in sera when stored on Gel Z in our serum separator tubes in comparison to a plain glass tube.

## **Study design:**

Two tube types were evaluated in this study:

- 16/100mm VACUETTE<sup>®</sup> Serum Gel (Gel Z) Tube, without clot activator
- plain glass tube as a reference

Three types of human serum pool are prepared with low, medium, and high concentration of the drug and mixed thoroughly. The terms "low, medium and high" are not nearer defined, because they depend on the described drug. Three tubes are prepared for each testing day. One ml of spiked serum pool each is filled into each open tube. The tubes are covered with parafilm and stored at 4°C.

Drug concentration is measured:

- immediately after adding the spiked serum pool to the tube
- after 1 day (storage at 4°C)
- after 3 days (storage at 4°C)

The analysis was performed on Dade Behring Dimension with the accompanying reagents, on Dynabott TDX with the accompanying reagents, and by ELISA.

The following 12 drugs were compared:

Arbekacin <sup>1)</sup>	Lidocaine <sup>1)</sup>
Bromperidol <sup>2)</sup>	Phenytoin <sup>3)</sup>
Carbamazepine <sup>3)</sup>	Phenobarbital <sup>3)</sup>
Digoxin <sup>3)</sup>	Theophylline <sup>3)</sup>
Disopyramide <sup>1)</sup>	Valproic Acid <sup>3)</sup>
Haloperidol <sup>2)</sup>	Vancomycin <sup>3)</sup>

<sup>1)</sup> Dynabott TDX <sup>2)</sup> ELISA <sup>3)</sup> Dade Behring Dimension  
The results in detail can be found in the Annex.

## **Results / Comments:**

Percent recovery was calculated and was expected to fall within +/-10% of the initial time control tube values. Values falling below 90% or above 110% recovery were considered clinically significant.

As shown in the table above, the antiepileptic Carbamazepine was below the 90% cut off at 24 hours. However, it has to be considered that the drug has a half-life of 12 – 24 hours. Stability of the drug on the gel up to 36 hours was shown for 11 out of the 12 drugs tested. These included the neuroleptics Bromperidol and Haloperidol, the cardiac glycoside Digoxin, the antiarrhythmic agent Disopyramide, the anaesthetic Lidocaine, the antiepileptics Phenytoin, Phenobarbital and Valproic acid, the antispasmodic Theophylline, and the antibiotics Vancomycin and Arbekacin.

## **Conclusion:**

The stability of therapeutic drugs in serum stored in gel tubes has been widely investigated. The absorption of drugs into the gel is dependent upon several factors including the chemical nature of the gel and of the drug itself, time on the gel, temperature of storage and volume of sample.

In this study the stability of 12 drugs added to a serum pool under laboratory conditions with low sample volumes has been examined. A small sample volume of 1 ml was used to exaggerate any absorption effects.

From the results, it can be concluded, that VACUETTE<sup>®</sup> Serum Gel Z tubes performed comparably with the plain tubes and that they are suitable for TDM analyses. Sample volumes greater than 1 ml will show greater recoveries than shown in this study.

## **References:**

(1) Dasgupta A., Yared M.A., Wells A., Time-dependent absorption of therapeutic drugs by the gel of the Greiner Vacuette blood collection tube. TherDrugMonit. (2000)

**Annex / Results in detail:**

drug	tube	concentration	recovery [%] after x store days		
			0	1	3
Arbekacin	plain glass tube	9,3 µg/ml	100,0	100,9	103,2
		11,2	100,0	104,9	100,9
		26,6	100,0	107,4	107,7
	Gel Z-tube	9,3	100,0	101,3	104,3
		11,2	100,0	103,7	108,6
		26,6	100,0	111,9	109,3
Bromperidol	plain glass tube	9,2 ng/ml	100,0	N/A	109,8
	Gel Z-tube	9,2	100,0	96,7	101,1
Carbamazepine	plain glass tube	4,0 µg/ml	100,0	100,0	105,0
		7,5	100,0	97,3	97,3
		11,2	100,0	101,8	97,3
	Gel Z-tube	4,0	100,0	102,5	105,0
		7,5	100,0	88,0	94,7
		11,2	100,0	105,4	98,2
Digoxin	plain glass tube	0,6 ng/ml	100,0	101,7	N/A
		0,9	100,0	101,1	104,5
		1,2	100,0	99,1	104,3
	Gel Z-tube	0,6	100,0	103,4	93,2
		0,9	100,0	103,4	105,6
		1,2	100,0	102,6	103,5
Disopyramide	plain glass tube	0,6 µg/ml	100,0	106,9	106,9
		2,2	100,0	101,8	100,0
		3,6	100,0	104,4	100,8
	Gel Z-tube	0,6	100,0	108,6	108,6
		2,2	100,0	99,1	96,4
		3,6	100,0	102,8	103,3
Haloperidol	plain glass tube	10,3 ng/ml	100,0	N/A	110,7
	Gel Z-tube	10,3	100,0	96,1	106,8
Lidocaine	plain glass tube	1,2 µg/ml	100,0	101,6	100,0
		3,2	100,0	99,7	102,5
		5,0	100,0	100,6	99,0
	Gel Z-tube	1,2	100,0	100,8	101,6
		3,2	100,0	101,2	98,1
		5,0	100,0	95,6	98,4
Phenytoin	plain glass tube	6,2 µg/ml	100,0	91,9	101,6
		8,6	100,0	108,1	103,5
		15,8	100,0	100,6	104,4
	Gel Z-tube	6,2	100,0	96,8	103,2
		8,6	100,0	105,8	107,0
		15,8	100,0	96,8	107,0
Phenobarbital	plain glass tube	9,3 µg/ml	100,0	93,5	96,8
		11,2	100,0	99,1	108,0
		26,6	100,0	101,9	103,8
	Gel Z-tube	9,3	100,0	100,0	104,3
		11,2	100,0	105,4	108,0
		26,6	100,0	102,3	115,8
Theophylline	plain glass tube	7,2 µg/ml	100,0	98,6	94,4
		11,1	100,0	104,5	104,5
		19,5	100,0	93,8	101,5
	Gel Z-tube	7,2	100,0	94,4	100,0
		11,1	100,0	92,8	95,5
		19,5	100,0	90,3	102,1
Valproic Acid	plain glass tube	48,0 µg/ml	100,0	94,2	92,7
		76,8	100,0	97,0	102,6
		106,0	100,0	96,8	90,7
	Gel Z-tube	48,0	100,0	89,8	97,3
		76,8	100,0	94,8	98,4
		106,0	100,0	102,9	96,0
Vancomycin	plain glass tube	7,9 µg/ml	100,0	100,0	102,5
		11,9	100,0	105,9	106,7
		19,5	100,0	102,1	101,5
	Gel Z-tube	7,9	100,0	94,9	98,7
		11,9	100,0	105,0	100,8
		19,5	100,0	104,6	103,6