

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number: k042808

B. Purpose for Submission: Notification of intent to manufacture and market the device: BAYER ADVIA IMS Carbamazepine Assay with Calibrator.

C. Measurand: Carbamazepine

D. Type of Test: Competitive, homogenous, immunoassay with Chemiluminescence and paramagnetic particles.

E. Applicant: Bayer HealthCare LLC

F. Proprietary and Established Names: Proprietary name – ADVIA IMS Carbamazepine Assay. Common name – Carbamazepine

G. Regulatory Information:

1. Regulation section: Carbamazepine Assay - 21 CFR 862.3645,
Carbamazepine calibrator - 21 CFR 862.3200
2. Classification: Class II
Class II
3. Product code: Carbamazepine Assay – KLT
Carbamazepine Calibrator - DKB
4. Panel: Toxicology (91)

H. Intended Use:

1. Intended use(s): The Bayer ADVIA IMS Carbamazepine is for in vitro diagnostic use to measure the antiepileptic drug Carbamazepine in human serum and plasma. Measurements of Carbamazepine (5H-Dibenz[b,f]azepine-5-carboxamide) are used as an aid in the diagnosis and treatment of Carbamazepine overdose, and in monitoring therapeutic levels of Carbamazepine to ensure appropriate therapy.
2. Indication(s) for use: The Bayer ADVIA IMS Carbamazepine is for in vitro diagnostic use to measure the antiepileptic drug Carbamazepine in human serum and plasma. Measurements of Carbamazepine (5H-Dibenz[b,f]azepine-5-carboxamide) are used as an aid in the diagnosis

and treatment of Carbamazepine overdose, and in monitoring therapeutic levels of Carbamazepine to ensure appropriate therapy.

3. Special conditions for use statement(s): For prescription use only.
4. Special instrument requirements: The BAYER ADVIA IMS Carbamazepine assay and calibrator are intended for use on the Bayer ADVIA IMS Analyzer.

I. Device Description: The Bayer ADVIA IMS Carbamazepine is for in vitro diagnostic use to measure the antiepileptic drug Carbamazepine in human serum **and plasma. Measurements of Carbamazepine (5H-Dibenz[b,f]azepine-5-carboxamide)]** are used as an aid in the diagnosis and treatment of Carbamazepine overdose, and in monitoring therapeutic levels of Carbamazepine to ensure appropriate therapy.

The device consists of liquid reagent used only on the Bayer ADVIA IMS for the determination of quantitative Carbamazepine results. Sold separately are liquid calibrators based on human serum with clinically significant levels of valproic acid added. These calibrators are tested and shown to be non-reactive for HBsAg, HIV, and anti-HCV using FDA approved tests.

J. Substantial Equivalence Information:

1. Predicate device name(s): ADVIA Centaur Carbamazepine assay.
2. Predicate 510(k) number(s): k964765
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	The Bayer ADVIA IMS Carbamazepine is for in vitro diagnostic use to measure the antiepileptic drug Carbamazepine in human serum and plasma. Measurements of Carbamazepine (5H-Dibenz[b,f]azepine-5-carboxamide)] are used as an aid in the diagnosis and treatment of Carbamazepine overdose, and in monitoring therapeutic levels of Carbamazepine to ensure appropriate therapy.	For in vitro diagnostic use in the determination of Carbamazepine in blood or serum using the Bayer CENTAUR system.

Similarities		
Item	Device	Predicate
Principle	Competitive, homogenous, immunoassay with Chemiluminescence and paramagnetic particles.	Competitive, homogenous, immunoassay with Chemiluminescence and paramagnetic particles.
Reagents	Similar	Two liquid reagents contained in system specific packaging
Storage	2-8 °C	2-8 °C
Differences		
Stability	30 days on system	28 days on system
Calibrator	Six Level calibration	Two level calibration

K. Standard/Guidance Document Referenced (if applicable):

NCCLS - How to define, determine, and utilize reference intervals in the clinical laboratory, C28-A.

NCCLS - Precision Performance of clinical chemistry devices, EP5-A.

NCCLS - Method comparison and bias using patient samples, EP9-A.

NCCLS - Procedures for the handling and processing of blood samples, H18-A2.

NCCLS – Interference testing in clinical chemistry, EP7-P.

L. Test Principle: The BAYER ADVIA IMS Carbamazepine is based upon established competitive, homogenous, immunoassay with Chemiluminescence and paramagnetic particles.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

- a. *Precision/Reproducibility:* Within run and total run imprecision were evaluated for ten days by testing three levels of commercially available Bayer Ligand Controls. The imprecision study was performed on system B23 for ten days with two runs per day and two cups per run. The Day 1 calibration was used for all runs. Within run and Total Imprecision was calculated using analysis of variance.

Imprecision Data

Product	Days	Runs	N	Mean µg/mL	Within Run		Total	
					SD	%CV	SD	%CV
Ligand Control 1	10	20	79	2.6	0.1	2.6	0.1	4.6
Ligand Control 2	10	20	80	5.6	0.1	1.9	0.2	2.6
Ligand Control 3	10	21	80	9.2	2.0	2.0	0.2	2.5

b. *Linearity/assay reportable range*: 1 µg/mL up to Carbamazepine concentration in highest calibrator (Level 6) (20.0 µg/mL). The linearity of this method was evaluated by comparing the recovery of the six level Carbamazepine calibrators as unknowns. Recoveries ranged from 110 % at 1 µg/mL to 101 % at 20 µg/mL.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods)*: The calibrators are human serum based and stored at 2 - 8 °C. The calibrators are traceable to an internal standard manufactured using highly purified material. Standard reference, SRM, Antiepilepsy Drug Level Assay Standard from the National Institute of Standards and Technology were evaluated and found to recover at 109% of target concentrations.

The stability of the IMS Carbamazepine Calibration is based on real time stability studies. Six lots of calibrators manufactured according to final production and quality assurance procedures were tested. The analyte was tested using a single instrument.

Vials from each lot were stored at the recommended temperature of 2 - 8 °C (test samples) for the duration of the studies. At approximately 3 month intervals, samples of the test vials were tested for the recovery of Carbamazepine. Based on results from 6 lots, the product was assigned 18 months stability.

d. *Detection limit*: The lowest detectable signal, as determined by subtracting two times the within run SD from the zero calibrator is 0.2 µg/mL.

e. *Analytical specificity*: Pooled serum samples with Carbamazepine levels of clinical significance were spiked with the compounds listed below. ADVIA Carbamazepine assay results from the spiked samples were compared with those of unspiked control samples. These compounds did not have a significant effect on the ADVIA

Carbamazepine measurement.

Compound
Amitriptyline
Carbamazepine- 10,11-epoxide
Ethosuximide
Phenobarbital
Phenytoin
Primidone
Valproic Acid
Chlorpromazine

Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with in vitro immunoassays. Patients routinely exposed to animals or animal serum products can be prone to this interference and value anomalies may be observed.

Interference was evaluated by spiking human serum pools with hemoglobin (from lysed human red blood cells, up to 600 mg/dL); unconjugated bilirubin (up to 25 mg/dL), conjugated bilirubin (up to 25mg/dL) and a triglyceride concentrate (Intralipid, up to 750 mg/dL). Intermediate dilutions were prepared by co-diluting the spiked sample with the unspiked sample. The observed recovery was considered to be of no clinical significance if the deviation for these potential interferences was $\leq 10\%$

f. Assay cut-off: N/A

2. Comparison studies:

a. *Method comparison with predicate device:* forty eight patient serum samples were tested on both the ADVIA IMS System and the Centaur System. The correlation is summarized as follows: $y = \text{ADVIA IMS}$, $x = \text{Centaur}$, Slope = 1.00, Intercept = 0.01, $S_{y.x} = 0.80$, $r = 0.988$, $n = 48$, IMS Range ($\mu\text{g/mL}$) 1.2 – 17.6.

b. *Matrix comparison:* The serum/plasma equivalency study was run on ADVIA IMS with matched human serum, heparinized plasma and EDTS-plasma samples. The results are summarized as follows.

Y	X	Slope	Intercept	$S_{y.x}$	R	N	IMS Range $\mu\text{g/mL}$
Heparinized Plasma	Serum	0.97	0.09	0.28	0.999	18	0.0 to 18.9
EDTA Plasma	Serum	1.00	-0.03	0.32	0.999	18	3.8 to 19.2

3. Clinical studies:

a. *Clinical Sensitivity:* N/A

b. *Clinical specificity:* N/A

c. Other clinical supportive data (when a. and b. are not applicable): N/A

4. Clinical cut-off: N/A

5. Expected values/Reference range: A therapeutic range of 16.9 – 50.8 $\mu\text{mol/L}$ (4 to 12 $\mu\text{g/mL}$) for serum and plasma has been reported for Carbamazepine. Toxic range is considered $>63.5(15)$. See Tietz N. W. Clinical Guide to Laboratory Tests. Philadelphia, PA, WB Saunders; 1995; 866-867.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion: The submitted information in this premarket notification is complete and supports a substantial equivalence decision.