510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
K032014

B. Analyte:
Immunoglobulin M (IgM)

C. Type of Test:
Quantitative, particle-enhanced immunonephelometry

D. Applicant:
Dade Behring Inc.

E. Proprietary and Established Names:
N Latex IgM

F. Regulatory Information:

1. Regulation section:
   21 CFR 866.5510, Immunoglobulins A, G, M, D and E immunological test system
2. Classification:
   Class II
3. Product Code:
   CFN, Method, Nephelometric, Immunoglobulins (G, A, M)
4. Panel:
   Immunology (82)

G. Intended Use:
In vitro diagnostic reagents for the quantitative determination of IgM in human cerebrospinal fluid (CSF) and in paired CSF/serum samples by means of particle-enhanced immunonephelometry using the BN™ Systems. The determination of IgM aids in the evaluation of the patient's immune system.

1. Indication(s) for use:
   In vitro diagnostic reagents for the quantitative determination of IgM in human cerebrospinal fluid (CSF) and in paired CSF/serum samples by means of particle-enhanced immunonephelometry using the BN™ Systems. The determination of IgM aids in the evaluation of the patient's immune system.
2. Special condition for use statement(s):
   Not applicable
3. Special instrument Requirements:
   Use with Dade Behring BN™ 100 (K892223), BN™ II (K943997) and BN ProSpec® Systems (K001647). These systems were 510(k) cleared and belong to the same instrument family with the same intended use and measuring method. Physical characteristics and operating features are also similar.

H. Device Description:
The device consists of N IgM Reagent, N IgM Standard, N IgM Control, N IgM, Supplementary Reagent A and Supplementary Reagent B. The N IgM Reagent are freeze-dried polystyrene particles coated with rabbit anti-human IgM antibody. The

N IgM Standard and Control reagents are freeze-dried mixture of human sera. The N Supplementary Reagent A is an aqueous solution of polyoxyethylene sorbitan monolaureate and the N IgM Supplementary Reagent B is combination of sheep anti-human IgG serum and human gamma globulin. The device is specific for the BN family of nephelometers.

I. Substantial Equivalence Information:

1. Predicate device name(s):
   Beckman Coulter IMMAGE® Immunochemistry System Low Concentration Immunoglobulin M (IGMLC) Assay
2. Predicate K number(s):
   K993547
3. Comparison with predicate:

DEVICE	PREDICATE
A. Similarities	
Intended Use. - Quantitative determination of IgM in human cerebrospinal fluid (CSF) and in paired CSF/serum samples	Quantitative determination of human immunoglobulin M in serum and cerebrospinal fluid by rate nephelometry
Sample Type – Serum or CSF	Serum or CSF
Instrumentation – Nephelometry (BN™ Systems)	Nephelometry (IMMAGE® Immunochemistry Systems)
B. Differences	
Test Principle – Measures intensity of scattered light as the result of aggregates formed by IgM in sample and IgM-coated polystyrene latex particles	Measures the rate of increase in light scattered from particles suspended in solution as a result of complexes formed during an antigen-antibody reaction.
Antibody – Polyclonal rabbit anti-human IgM	Polyclonal goat anti-human IgM
Measuring range - 0.27 - 8.6 g/L (serum) 0.13 – 4.2 mg/L (CSF)	0.1 – 12.98 g/L (serum) 0.3 – 60 mg/L (CSF)

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

None referenced.

K. Test Principle:

Polystyrene particles coated with anti-human IgM antibodies are aggregated when mixed with samples containing human IgM. These aggregates scatter a beam of light passing through the sample. The intensity of the scattered light is proportional to the concentration of IgM in the sample. The results are determined by comparison with an IgM standard of known concentration.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. Precision/Reproducibility:

Precision was determined using 3 CSF and 3 serum samples assayed in quadruplicates, 2 runs per day for 4 days and 1 run per day for 2 days. The results are acceptable for this type of assay and are summarized in the following table.

		Precision		
Type of Specimen	Mean value	Within-run	Between- run	Total
CSF	(mg/L)	CV (%)	CV (%)	CV (%)
Control	2.5	2.1	1.5	2.4
CSF Pool 1	0.56	5.5	2.3	5.3
CSF Sample	3.0	2.0	1.9	2.6
Serum	(g/L)			
Sample 1	0.81	4.9	2.7	5.0
Sample 2	1.5	3.8	2.3	4.0
Sample 3	7.7	2.4	2.0	3.0

b. Linearity/assay reportable range:
Linearity was determined by testing serial dilutions of a serum pool and a CSF pool containing high concentrations of IgM. Each dilution was tested in replicates of five. The range for serum was 0.34 to 8.2 g/L and for CSF, 0.15 to 3.64 mg/L. The mean % recovery for serum was 103% (98% to 111%) and for CSF was 94% (84% to 101%). Linear regression analysis yielded a slope of 0.996 and r = 1.0 for serum and a slope of 1.0 and r = 0.999 for CSF. The results met the established acceptance criteria and supported the linearity claims for both sample types.

The assay range is 0.13 to 4.2 mg/L for CSF and 0.27 to 8.6 g/L for serum (diluted to 1:2000).

c. Traceability (controls, calibrators, or method):
Controls and calibrators are traceable to the reference material CRM 470.

d. Detection limit (functional sensitivity):
Detection limit is defined as the lower limit of the reference curve and is dependent on the concentration of the IgM in the N IgM Standard. The limit of detection is 0.13 mg/L for CSF.

e. Analytical specificity:
Interference testing was performed using normal serum preparations spiked with varying concentrations of triglycerides (up to 1997 mg/dL), free hemoglobin (up to 1000 mg/dL) and total bilirubin (up to 60 mg/dL). No interference was observed with the concentrations tested.

f. Assay cut-off:
Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:
Initially the study included 50 CSF samples (IgM concentrations ranged from 0.19 to 5.48 mg/L) and 50 matched serum samples (IgM concentration ranged from 0.129 to 2.35 g/L). Twenty-six CSF

samples were excluded from the study because their IgM concentrations were outside the new device's measuring range. The remaining 24 CSF samples and the 50 serum samples were assayed with both new and predicate devices. The results were analyzed by Passing-Bablok regression analysis and summarized below.

Sample Type	N	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r)
CSF	24	1.04 (0.905, 1.25)	-0.0249 (-0.17, 0.0452)	0.9945
Serum	50	0.9108 (0.8629, 0.9533)	0.0228 (-0.0153, 0.0636)	0.9788
CSF/Serum Quotients	24	1.0285 (0.8926, 1.1881)	-0.0112 (-0.0890, 0.0546)	0.9889

b. Matrix comparison:
Not applicable.

3. Clinical studies:
   a. Clinical sensitivity:
   Not performed.
   b. Clinical specificity:
   Not performed.
4. Clinical cut-off:
   Not applicable.
5. Expected values/Reference range:
   The reference range was determined using 220 patients from Central Europe with normal albumin CSF/serum ration and with no evidence of inflammation. The upper limit of the reference range (95^{th} percentile) for IgM in CSF was 1.3 mg/L.

M. Conclusion:

Based on the review of information provided in this 510 (k), the analytical performance of the N Latex IgM assay correlated with the performance of the Beckman Coulter IMMAGE® IGMLC assay and therefore, demonstrate that the new device is substantially equivalent to the marketed device.