

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k071247

B. Purpose for Submission:

New device

C. Measurand:

Rheumatoid factor (RF)

D. Type of Test:

Particle enhanced nephelometry

E. Applicant:

Dade Behring, Inc.

F. Proprietary and Established Names:

N Latex RF Kit

G. Regulatory Information:

1. Regulation sections:
21 CFR 866.5775 Rheumatoid factor immunological test system
2. Classifications:
Class II
3. Product codes:
DHR System, test, rheumatoid factor
4. Panel:
Immunology (82)

H. Intended Use:

1. Intended use(s):
Quantitative determination of rheumatoid factors (RF) in human serum, lithium heparin and EDTA plasma on the BN™ II and BN ProSpec® Systems as an aid in the diagnosis of rheumatoid arthritis.
2. Indication(s) for use:
Same as the Intended Use
3. Special conditions for use statement(s):
Prescription use
4. Special instrument requirements:
BN II or BN ProSpec Systems

I. Device Description:

The device consists of N RF Reagent: a suspension of polystyrene particles coated with an immunocomplex of human- γ -globulin/anti-human- γ -globulin from sheep; and N RF Supplement: an aqueous solution of polyethylene glycol containing detergent.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Dade Behring N RF Latex
2. Predicate 510(k) number(s):
k942328

3. Comparison with predicate:

Similarities		
Item	New Device	Predicate
	N Latex RF Kit	N Latex RF
Indications for use	Aid in the diagnosis of rheumatoid arthritis	Same
Methodology	Nephelometry	Same
Capture	Immunocomplex of human- γ -globulin/sheep anti-human- γ -globulin	Same
Calibrator referenced to:	N Rheumatology Standard SL and 1 st British Standard 64/0023	Same
Reportable range	10-640 IU/mL	Same

Differences		
Item	New Device	Predicate
Reagents	N RF Reagent – <i>liquid</i> and N RF Supplement Reagent - liquid	N RF Reagent – <i>lyophilized</i> and N RF Supplementary Reagent - liquid
Sample type	Serum	Serum, lithium heparin or EDTA plasma
Analyzer	BN Systems	BN II and BN ProSpec Systems

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

CLSI EP5-A2 *Evaluation of Precision Performance of Quantitative Measurement Methods*; Approved Guideline-Second Edition; and CLSI EP7-A2 *Interference Testing in Clinical Chemistry*; Approved Guideline-Second Edition

L. Test Principle:

Polystyrene particles coated with an immunocomplex consisting of human immunoglobulin and anti-human IgG from sheep are aggregated when mixed with samples containing RF. These aggregates scatter a beam of light passed through the sample. The intensity of the scattered light is proportional to the concentration of the protein in the sample. The result is evaluated by comparison with a standard of known concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

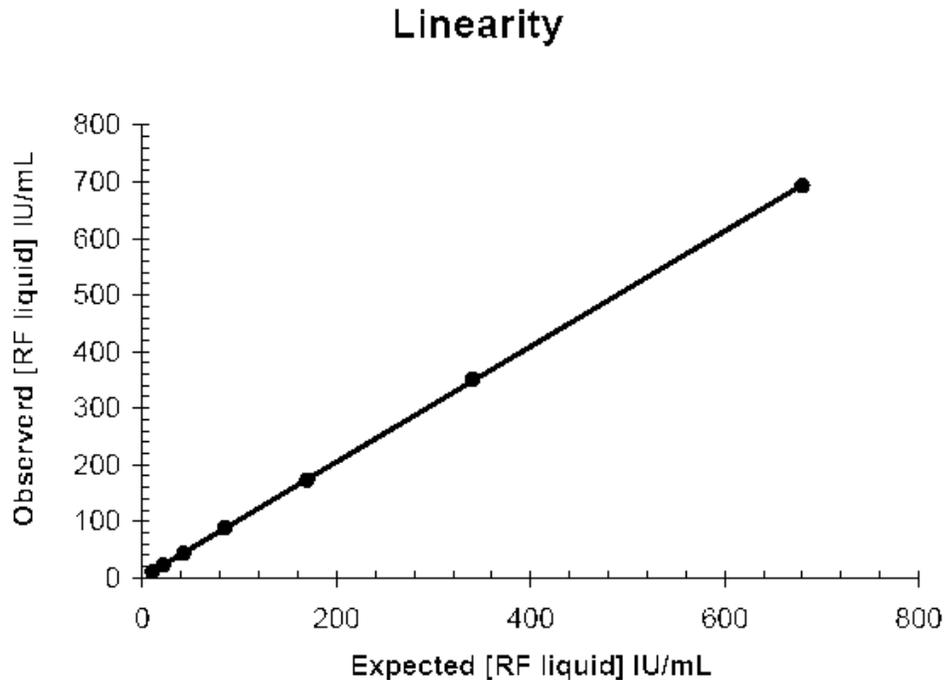
a. *Precision/Reproducibility:*

Precision testing was performed on a BN II System in accordance with CLSI EP5-A2. Specimens at each level were analyzed in duplicate, twice a day, for 20 days. The repeatability, between-run and within-lab %CVs were calculated by the analysis of variance method.

Sample	Mean IU/mL	Repeatability %CV	Between Run %CV	Within Lab %CV
Control SL/1	69.3	2.2	5.2	5.7
Control SL/2	170.2	2.2	3.1	3.8
Serum pool low 1	27.9	2.7	5.4	7.9
Serum pool low 2	81.3	2.2	4.8	5.3
Serum pool high 1	582.7	5.1	4.8	7.7
Serum pool high 2	600.8	5.3	5.8	8.1

b. Linearity/assay reportable range:

Linearity across the assay range (approximately 10 to 640 IU/mL) was confirmed by testing an internal, high standard. The standard was serially diluted with System Diluent down to the lower measuring range (693.2 down to 10.8 IU/mL) on a BN II Analyzer. Each dilution was tested in replicates of three. Data were analyzed using linear regression analysis. The slope was 1.021, intercept 0.665 and $r = 1.00$.



Hook Effect: The possibility of hook effect occurring was evaluated with a

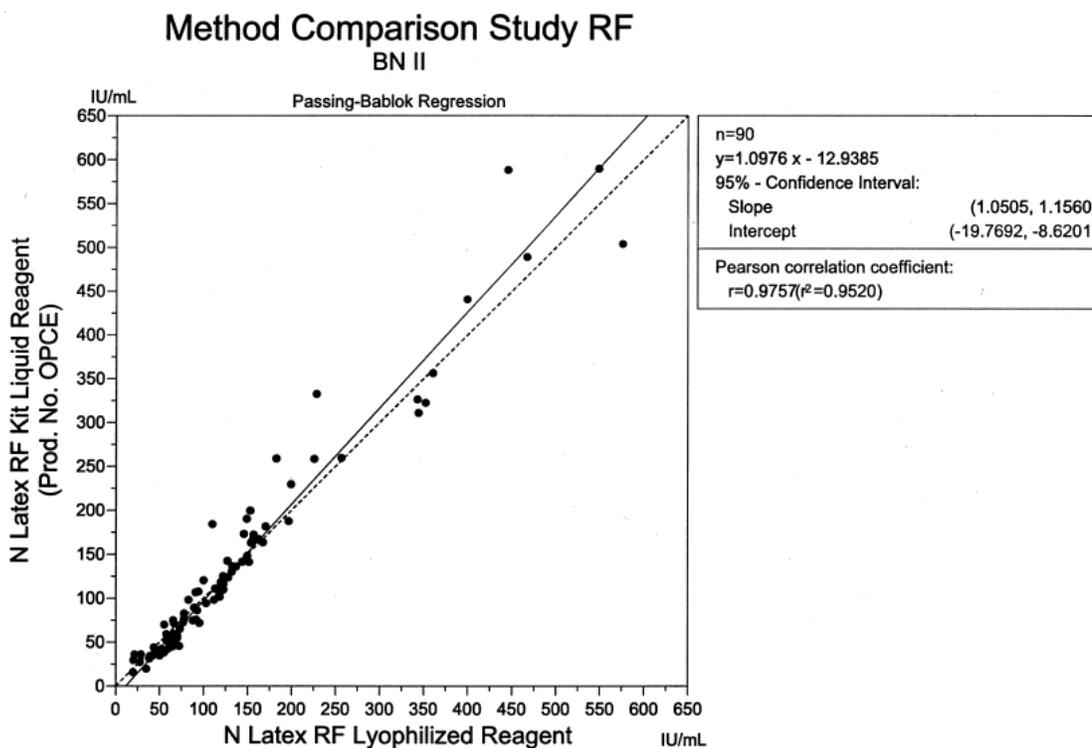
serum sample above the assay range. The sample was serially diluted and analyzed on the BN II analyzer and demonstrated no hook effect up to 3967 IU/mL.

- c. Traceability, Stability, Expected values (controls, calibrators, or methods):
The calibrator is standardized against the N Rheumatology Standard SL and 1st British Standard 64/0023.
- d. Detection Limit/Analytical Sensitivity:
The analytical sensitivity of the assay was determined by the lower limit of the reference curve (approximately 10 IU/mL).
- e. Analytical specificity:
Interference testing was performed according to CLSI EP7-A2 to determine the effect of bilirubin (0.6 g/L) and hemoglobin (10/g/L). Testing was conducted by running a serum sample without the interferant and comparing it to the value obtained from the same sample to which the potential interferant had been added. For each spiked sample, the % recovery was determined. Percent recoveries ranged from 92.3 to 100.7% in the bilirubin spiked samples and from 89.7 to 95.6% for hemoglobin
- f. Assay cut-off:
Testing of serum from 253 adult European blood donors resulted in a 97.5th percentile of 15.9 IU/mL.

2. Comparison studies:

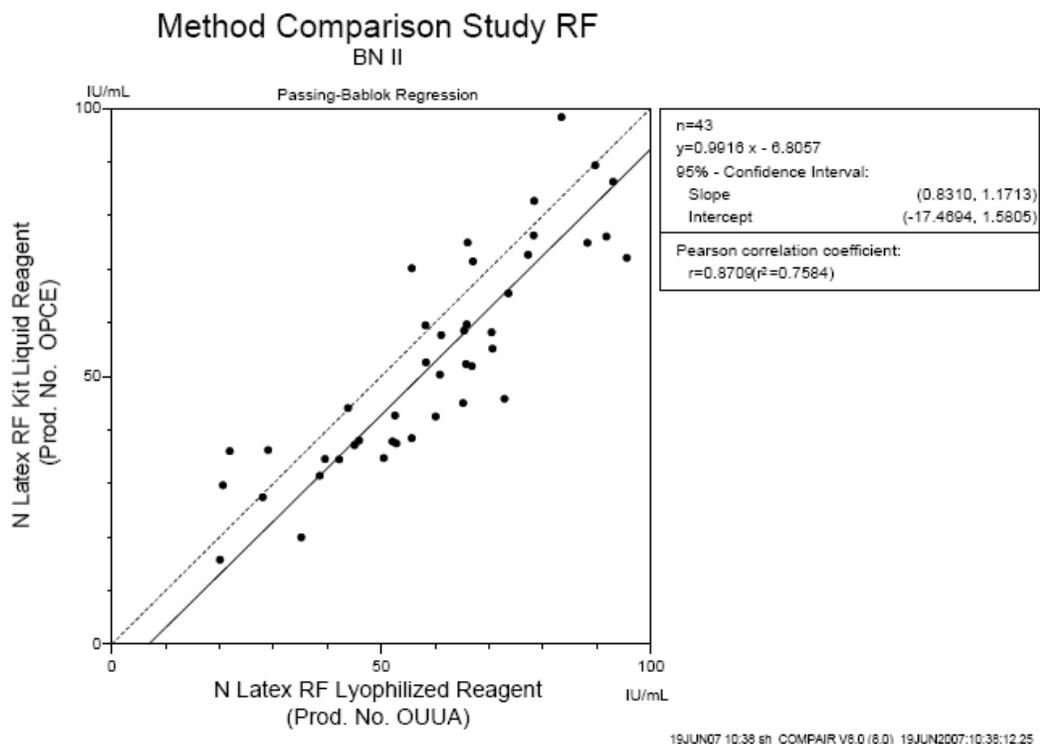
- a. *Method comparison with predicate device:*

Serum samples from 90 subjects were tested on the BN II analyzer.



Parameter:	95% confidence interval	
N = 90 (15.8 – 598.8 IU/mL)		
Slope	1.098	1.0505, 1.1560
Intercept	-12.94	-19.7692, -8.6201
Pearson correlation coefficient	r=0.9757 (r ² =0.9520)	

For samples with results <100 IU/mL:



Parameter:	95% confidence interval	
N=43 (20 – 78.3)		
Slope	0.9916	0.8310, 1.1713
Intercept	-6.8057	-17.4694, 1.5805
Pearson correlation coefficient	r=0.8709 (r ² =0.7584)	

b. Matrix comparison:

A comparison was performed with matched specimens of serum, lithium heparin (n=111) and EDTA (n=33) plasma. Passing-Bablok regression analyses showed the following:

Serum vs. lithium heparin plasma

Parameter:	95% confidence interval	
N = 111 (14.5 – 533 IU/mL)		
Slope	0.963	0.949, 0.977
Intercept	0.928	-0.767, 2.221
Pearson correlation coefficient	r=0.992 (r ² =0.984)	

Serum vs. EDTA plasma (n=33)

Parameter:	95% confidence interval	
N = 33 (19.1 – 527 IU/mL)		
Slope	0.957	0.923, 0.998
Intercept	-12.94	-3.670, 1.659
Pearson correlation coefficient	r=0.997 (r ² =0.994)	

- c. *Behring ProSpec analyzer (k001647) compared to the BN II analyzer*
 The Performance Study Protocol included method comparison and precision. Between run %CVs ranged from 1.1 to 5.3% and within lab ranged from 2.2 to 6.3%. The linearity studies showed a slope of 0.98 and r = 1.0. The two instruments were compared by testing 86 samples ranging from 18.7 to 510.3 IU/mL. The comparison showed the following: $y = 1.1 - 13.4$, $r = 0.99$. Established acceptance criteria were met.

3. Clinical studies:

- a. *Clinical Sensitivity:*

Not determined

- b. *Clinical specificity:*

Not determined

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

Not applicable

4. Clinical cut-off:

Not determined

5. Expected values/Reference range:

The expected value in the normal population is negative. However, apparently healthy asymptomatic individuals may have RF, usually of low titer. The incidence of false positive increases with age and is similar in females and males.

N. Proposed Labeling:

The labeling is sufficient and 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.