Design Verification

CRP (C-REACTIVE PROTEIN)
Multipurpose Reagent

CONTENTS

1 Introduction

The performance characteristics of CRP (C-reactive protein) multipurpose reagent were tested and documented in order to verify the clinical usefulness and compliance with the essential requirements of directive 98/79/EC.

CRP multipurpose reagent are filled in original HUMAN reagent plastic bottles. For use on automated analyzers the CRP multipurpose reagent must be refilled in analyzer-specific reagent bottles.

REF	Name	Content	Calibration type	Added performance data
11241	CRP	1 x 10 ml Antiserum 1 x 40 ml Buffer	1-point calibration	Imprecision, linearity, detection limit, method comparison, and stability data
			multi-point calibration	Imprecision, linearity, detection limit, method comparison, and stability data
11141	CRP Buffer	4 x 100 ml	1-point and multi-point calibration	Recovery, linearity

Material

Analyzer	Manufacturer	REF
AU 400	Beckman Coulter	N1254600
AU 480	Beckman Coulter	N3660400
HumaStar 600	HUMAN	16660

2 Imprecision

2.1 Imprecision within-run and day to day – multi-point calibration

The imprecision within-run / intra-assay for CRP on AU 400 was calculated from 20 determinations. The imprecision day-to-day / inter-assay was calculated by the means of 2 determinations on 20 consecutive days. 3 pool serum were employed as sample material.

Criteria

Imprecision	Acceptance criteria
Within-run	CV ≤ 7%
Day-to-day	CV ≤ 8 %

Used Material

Reagent	Manufacturer	REF	LOT
CRP	HUMAN	11241	
CRP Standard	HUMAN	11341	16005
Samples	3 pool serum: CEN02, CEN03, CEN04 and LIN-pool		

Results

Imprecision within-run	Measured concentration (mg/l)		
Replicates	Low	Medium	High
1	5.97	12.6	39.4
2	6.70	12.4	39.8
3	6.42	12.1	39.8
4	6.40	12.5	39.5
5	7.08	12.4	38.7
6	6.44	12.5	39.5
7	6.46	12.4	38.6
8	6.39	12.3	38.8
9	6.32	11.8	38.4

10	6.10	12.7	38.9
11	6.91	12.6	38.7
12	6.74	13.3	38.9
13	5.65	12.6	38.8
14	6.03	12.5	38.8
15	6.25	12.1	38.2
16	5.62	12.1	38.9
17	6.25	12.1	37.9
18	6.53	12.0	38.5
19	6.64	12.1	37.8
20	6.44	12.2	38.3
Mean	**6.37**	**12.4**	**38.8**
SD	0.37	0.32	0.57
CV%	**5.8**	**2.6**	**1.5**

Results

Imprecision day-to-day	Measured concentration (mg/l)								
	Low			Medium			High		
Day	Result 1	Result 2	Mean	Result 1	Result 2	Mean	Result 1	Result 2	Mean
1	5.97	6.70	6.34	12.6	12.4	12.5	39.4	39.8	39.6
2	6.65	6.34	6.50	12.7	12.0	12.3	38.5	38.7	38.6
3	6.30	6.06	6.18	12.4	11.7	12.0	38.5	38.2	38.3
4	5.87	6.17	6.02	12.8	12.1	12.4	38.5	37.7	38.1
5	5.92	5.99	5.96	11.5	12.4	11.9	37.8	37.9	37.8
6	5.43	5.98	5.71	11.6	11.3	11.5	37.9	37.9	37.9
7	6.36	6.08	6.22	12.1	11.9	12.0	38.1	37.1	37.6
8	5.93	5.77	5.85	10.8	11.3	11.1	37.6	37.2	37.4
9	5.80	5.71	5.76	11.9	11.7	11.8	37.4	38.3	37.9
10	6.20	5.16	5.68	11.1	11.2	11.2	37.9	37.2	37.5
11	6.13	6.22	6.18	11.5	11.7	11.6	37.3	38.1	37.7
12	5.93	6.10	6.02	11.4	11.0	11.2	37.8	38.2	38.0
13	6.18	6.09	6.14	11.9	11.9	11.9	38.2	38.8	38.5
14	6.43	5.57	6.00	11.7	11.9	11.8	37.8	37.7	37.8
15	5.98	5.86	5.92	11.5	10.1	10.8	38.6	38.1	38.3
16	5.71	6.02	5.87	11.7	11.2	11.4	37.1	37.1	37.1
17	5.48	5.74	5.61	11.4	10.9	11.2	38.4	37.0	37.7
18	5.94	5.35	5.65	10.7	11.3	11.0	37.1	37.0	37.1
19	5.69	5.96	5.83	11.9	11.4	11.7	37.6	37.6	37.6
20	5.51	5.28	5.40	11.4	10.0	10.7	37.4	37.3	37.3
Mean			**5.94**			**11.6**			**37.9**
SD			0.27			0.53			0.58
CV%			**4.5**			**4.6**			**1.5**

Conclusion

For CRP multipurpose reagent on AU 400 fullfilled the within-run / intra-assay and day-to-day / inter-assay precision acceptance criteria in the low (~ 6 mg/l), medium (~12 mg/l) , and high (~38 mg/l) concentration range: CV% 7 and 8, respectively.

2.2 Imprecision within-run and day-to-day – 1-point calibration

The imprecision day-to-day / inter-assay of CRP on AU 400 was calculated from 6 determinations on 5 consecutive days. 3 pool serum were employed as sample material.

Criteria

Imprecision	Acceptance criteria

Within-run	CV ≤ 10 %
Day-to-day	CV ≤ 10 %

Used Material

Reagent	**Manufacturer**	**REF**	**LOT**
CRP	HUMAN	11241	n/a
CRP Standard	HUMAN	11341	n/a
Samples	3 pool serum		

Results

Mean analyte concentration (mg/l)	**Intra-assay**		**Inter-assay**	
	SD (mg/l)	**%CV**	**SD (mg/l)**	**%CV**
3.96	0.14	**3.54**	0.42	**10.6**
8.52	0.19	**2.23**	0.45	**5.32**
40.5	0.34	**0.84**	0.58	**1.43**

Conclusion

CRP multipurpose reagent on AU 400 fullfilled the within-run / intra-assay and day-to-day / inter-assay precision acceptance criteria (CV ≤ 10%) in the low, medium and high concentration range, except of one result for day-to-day / inter-assay precision in the low concentration range (3.96 mg/l), which is below the cut-off value 5 mg/l.

3 Linearity, Sensitivity and Prozone Effect

3.1 Linearity – multi-point calibration – CRP kit

The linearity of CRP on AU 400 was controlled by employing a high concentrated pool serum successively with physiological saline. The analysed concentrations were compared with the calculated concentrations obtained from a linear regression.

Criteria

Linearity	**Acceptance criteria**
Deviation from regression line	≤ 10%

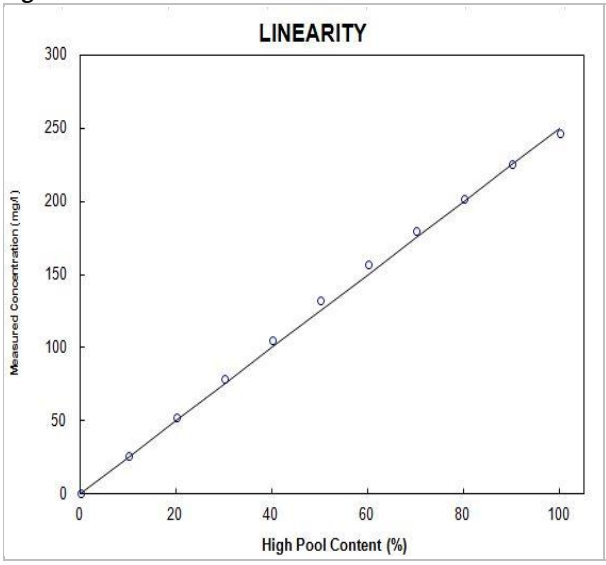
Used Material

Reagent	**Manufacturer**	**REF**	**LOT**
CRP	HUMAN	11241	0001
CRP Standard	HUMAN	11341	16005
Sample	Pool serum, LOT CEN01		

Results

High Pool Content	**Analytical Data**	**Regressed Data**	**Deviation from Regression Line**	
(%)	**mg/l**	**mg/l**	**mg/l**	**%**
0	1.46	0.00	1.46	
10	27.0	25.0	2.0	7.8
20	53.3	50.0	3.3	6.6
30	79.3	75.0	4.3	5.7
40	106	100	6	5.7
50	133	125	8	6.3
60	157	150	7	4.8
70	180	175	5	3.1
80	202	200	2	1.0
90	226	225	1	0.4
100	247	250	-3	-1.2

Figure



Linear up to 150 mg/l at least

3.2 Linearity – multi-point calibration – CRP kit and CRP buffer kit

The linearity of CRP on HumaStar 600 was controlled by employing a high concentrated pool serum successively with physiological saline. For this study, combinations of different antiserum and buffer LOTs were tested: 3 LOTs of CRP antiserum and 1 LOT CRP buffer. The analysed concentrations were compared with the calculated concentrations obtained from a linear regression.

Criteria

Linearity	**Acceptance criteria**
Deviation from regression line	≤ 10%

Used Material

Reagent	**Manufacturer**	**REF**	**LOT**
CRP antiserum	HUMAN	11241	0045, 0053, 0054
CRP buffer	HUMAN	11141	CEN081
CRP Standard	HUMAN	11341	17003
Sample	Pool serum, LOT CEN180		

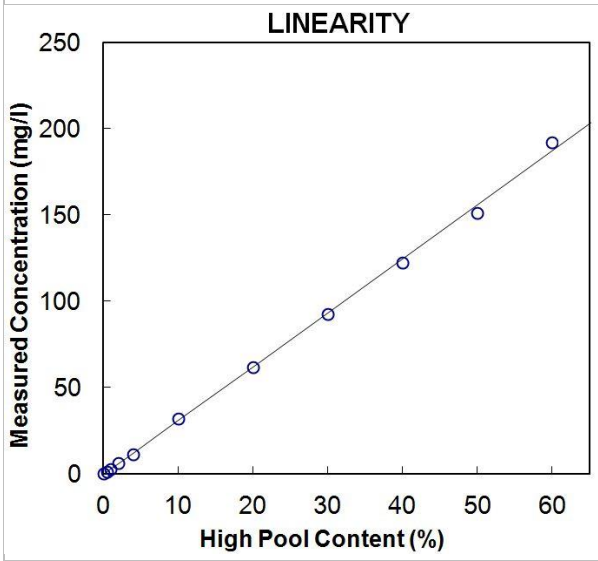
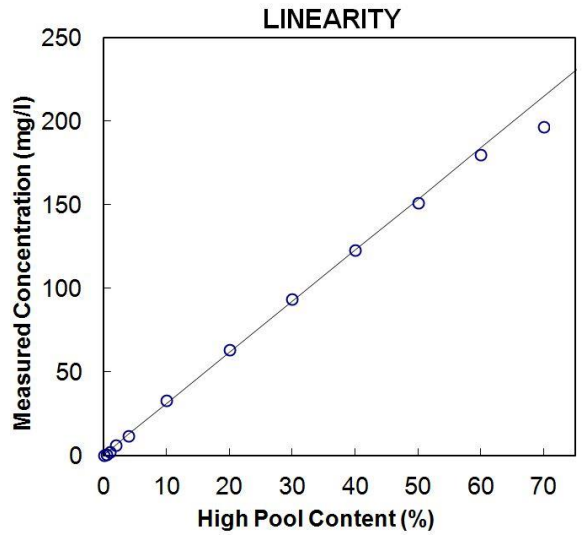
Results

CRP antiserum, LOT 0045, CRP buffer LOT CEN081				
High Pool Content	**Analytical Data**	**Regressed Data**	**Deviation from Regression Line**	
(%)	**mg/l**	**mg/l**	**mg/l**	**%**
0	0.20	-0.49	0.69	
10	32.0	30.8	1.2	4.0
20	62.1	62.0	0.1	0.1
30	92.6	93.3	-0.7	-0.8
40	122	125	-2	-1.7
50	151	156	-4	-2.8
60	192	187	5	2.8

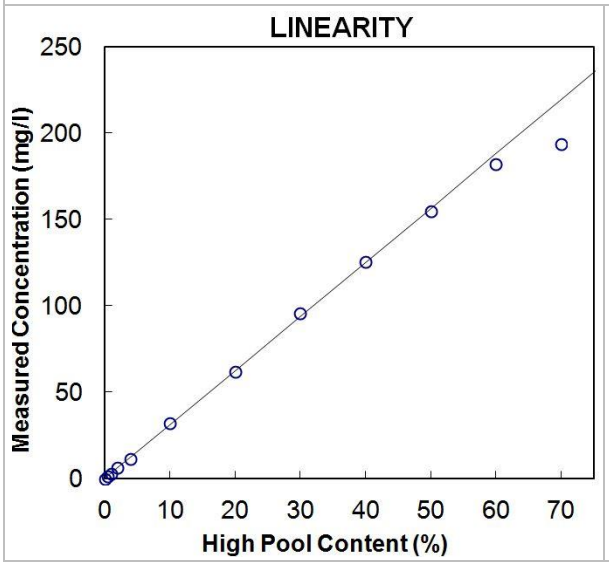
CRP antiserum, LOT 0053, CRP buffer LOT CEN081				
High Pool Content	Analytical Data	Regressed Data	Deviation from Regression Line	
(%)	mg/l	mg/l	mg/l	%
0	0.10	0.35	-0.25	
10	33.1	31.0	2.1	6.9
20	63.3	61.5	1.7	2.8
30	93.7	92.1	1.5	1.6
40	123	123	0	0.2
50	151	153	-2	-1.4
60	180	184	-4	-2.3
70	197	215	-18	-8.3

CRP antiserum, LOT 0054, CRP buffer LOT CEN081				
High Pool Content	Analytical Data	Regressed Data	Deviation from Regression Line	
(%)	mg/l	mg/l	mg/l	%
0	0.10	-0.06	0.16	
10	32.1	31.2	0.9	2.8
20	62.1	62.5	-0.4	-0.7
30	95.8	93.8	1.9	2.0
40	126	125	1	0.5
50	155	156	-2	-1.0
60	182	188	-5	-2.9
70	194	219	-25	-11.4

Figure

CRP antiserum, LOT 0045, CRP buffer LOT CEN081	CRP antiserum, LOT 0053, CRP buffer LOT CEN081
	
Linear up to 150 mg/l	Linear up to 150 mg/l

CRP antiserum, LOT 0054, CRP buffer LOT CEN081



Linear up to 150 mg/l

3.3 Linearity – 1-point calibration – CRP kit

The linearity of CRP on AU 400 was controlled by employing a high concentrated pool serum successively diluted with physiological saline. The analysed concentrations were compared with the calculated concentrations obtained from a linear regression.

Criteria

Linearity	Acceptance criteria
Deviation from regression line	≤ 10%

Used Material

Reagent	Manufacturer	REF	LOT
CRP	HUMAN	11241	0001
CRP Standard	HUMAN	11341	16005
Sample	Diluted high concentrated serum pool: CEN01		

Results

High Pool Content	Analytical Data	Regressed Data	Deviation from Regression Line	
(%)	mg/l	mg/l	mg/l	%
0	0.48	8.00	-7.53	
10	32.5	32.2	0.3	0.8
20	60.7	56.4	4.3	7.7
30	85.1	80.6	4.5	5.6
40	107	105	2	2.0
50	132	129	3	2.1
60	152	153	-1	-0.9
70	174	177	-3	-1.8
80	196	202	-5	-2.6
90	215	226	-11	-4.8
100	236	250	-14	-5.7

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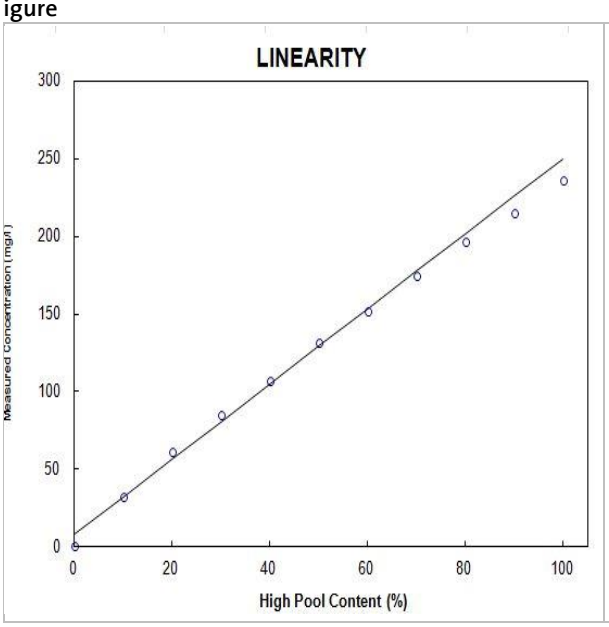
	Linear up to 190 mg/l under consideration of the data from the real time stability

3.4 Linearity – 1-point calibration – CRP kit and CRP buffer kit

The linearity of CRP on AU 480 was controlled by employing a high concentrated pool serum successively with physiological saline. For this study, combinations of different antiserum and buffer LOTs were tested: 3 LOTs of CRP antiserum and 1 LOT CRP buffer. The analysed concentrations were compared with the calculated concentrations obtained from a linear regression.

Criteria

Linearity	**Acceptance criteria**
Deviation from regression line	≤ 10%

Used Material

Reagent	**Manufacturer**	**REF**	**LOT**
CRP antiserum	HUMAN	11241	0045, 0053, 0054
CRP buffer	HUMAN	11141	CEN081
CRP Standard	HUMAN	11341	17003
Sample	Pool serum, LOT CEN180		

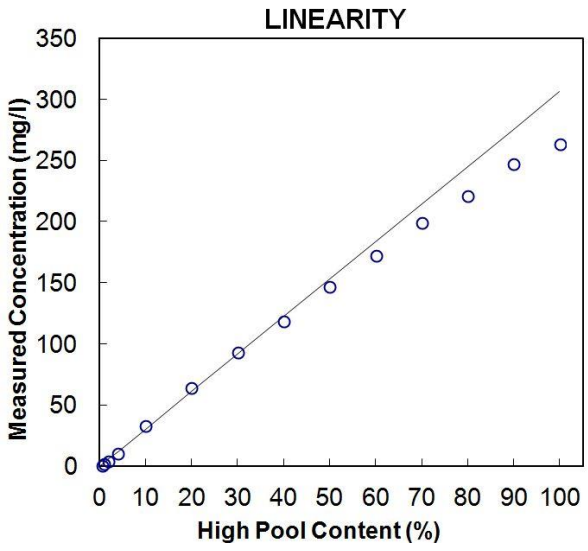
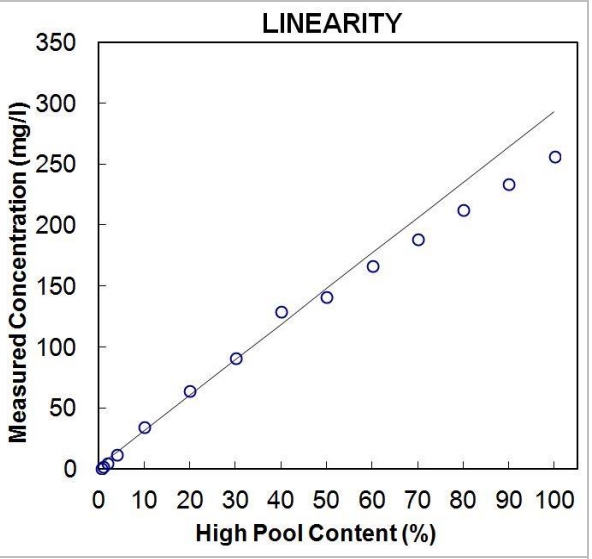
Results

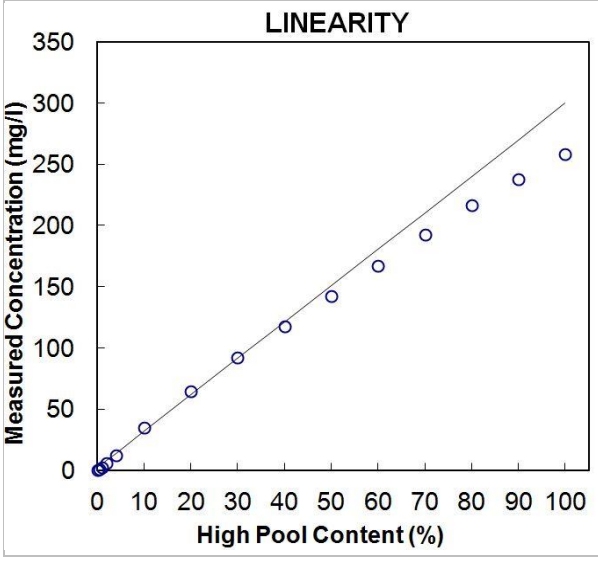
CRP antiserum, LOT 0045, CRP buffer LOT CEN081				
High Pool Content	Analytical Data	Regressed Data	Deviation from Regression Line	
(%)	mg/l	mg/l	mg/l	%
0	-0.38	-0.30	-0.08	
10	33.4	30.3	3.0	10.0
20	64.0	61.0	3.1	5.0
30	93.0	91.6	1.4	1.5
40	119	122	-3	-2.8
50	147	153	-6	-4.0
60	172	183	-11	-6.2
70	199	214	-15	-6.9
80	221	245	-24	-9.7
90	247	275	-28	-10.3
100	264	306	-42	-13.8

CRP antiserum, LOT 0053, CRP buffer LOT CEN081				
High Pool Content	Analytical Data	Regressed Data	Deviation from Regression Line	
(%)	mg/l	mg/l	mg/l	%
0	-0.16	2.30	-2.46	
10	34.5	31.4	3.1	9.8
20	64.0	60.4	3.5	5.8
30	91.0	89.5	1.5	1.7
40	129	119	11	9.0
50	142	148	-6	-4.2
60	166	177	-10	-5.9
70	188	206	-18	-8.5
80	212	235	-22	-9.5
90	234	264	-30	-11.5
100	257	293	-36	-12.4

CRP antiserum, LOT 0054, CRP buffer LOT CEN081				
High Pool Content	Analytical Data	Regressed Data	Deviation from Regression Line	
(%)	mg/l	mg/l	mg/l	%
0	0.01	2.10	-2.10	0.01
10	35.0	31.9	3.1	9.8
20	64.8	61.6	3.2	5.2
30	91.9	91.4	0.5	0.6
40	118	121	-4	-2.9
50	142	151	-9	-5.8
60	167	181	-13	-7.4
70	192	210	-18	-8.6
80	216	240	-24	-9.9
90	238	270	-32	-11.8
100	259	300	-41	-13.7

Figure

CRP antiserum, LOT 0045, CRP buffer LOT CEN081	CRP antiserum, LOT 0053, CRP buffer LOT CEN081
	
Linear up to 200 mg/l	Linear up to 200 mg/l

CRP antiserum, LOT 0054, CRP buffer LOT CEN081	
	Linear up to 200 mg/l

Conclusion

The linearity of CRP multipurpose reagent was found as follows:

Calibration type	CRP kit REF 11241	CRP kit, REF 11241, used with Buffer kit, REF 11141
CRP, multi-point calibration*	linear up to 150 mg/l	linear up to 150 mg/l
CRP, 1-point calibration	linear up to 250 mg/l	linear up to 200 mg/l

*For the multipoint calibration the upper linearty range depends on the LOT specific concentration of CRP Standard.

3.5 Sensitivity – multi-point calibration

The limit of detection (LoD) of CRP on AU 400 was evaluated form a 20-fold determination of physiological saline. The concentrations were manually calculated from the absorbance values. The LoD was calculated as follows: result mean + 3 SD.

Material

Reagent	Manufacturer	REF	LOT
CRP	HUMAN	11241	0001
CRP Standard	HUMAN	11341	16005
Sample	physiological saline		

Results

Absorbance values	Calculated Result mg/l
0.0015	1.27
0.0012	1.02
0.0018	1.44
0.0008	0.78
0.0013	1.14
0.0014	1.19
0.0011	0.97
0.0018	1.45
0.0006	0.62
0.0011	0.96

0.0013	1.13
0.0017	1.38
0.0009	0.84
0.0013	1.10
0.0014	1.20
0.0019	1.53
0.0019	1.53
0.0011	0.99
0.0016	1.33
0.0017	1.41
Mean	**1.16**
SD	0.26
LoD	**1.94**

3.6 Sensitivity – 1-point calibration

The limit of detection (LoD) of CRP on AU 400 was evaluated form a 20-fold determination of physiological saline. The concentrations were manually calculated from the absorbance values. The LoD was calculated as follows: result mean + 3 SD.

Material

Reagent	**Manufacturer**	**REF**	**LOT**
CRP	HUMAN	11241	0001
CRP Standard	HUMAN	11341	16005
Sample	physiological saline		

Results

Absorbance values	**Calculated Result mg/l**
0.0006	0.36
0.0009	0.53
-0.0003	-0.16
0.0003	0.16
0.0006	0.32
0.0006	0.37
0.0007	0.41
0.0001	0.06
0.0008	0.48
0.0011	0.62
0.0005	0.28
0.0000	-0.02
0.0000	0.02
0.0002	0.10
0.0002	0.10
0.0006	0.32
0.0009	0.51
0.0000	-0.03
0.0003	0.17
0.0010	0.56
Mean	**0.26**
SD	0.22
LoD	**0.93**

Conclusion

The limit of detection (LoD) of CRP multipurpose reagent on AU 400 was found:
CRP – multi-point calibration: 2 mg/l
CRP – 1-point calibration: 1 mg/l

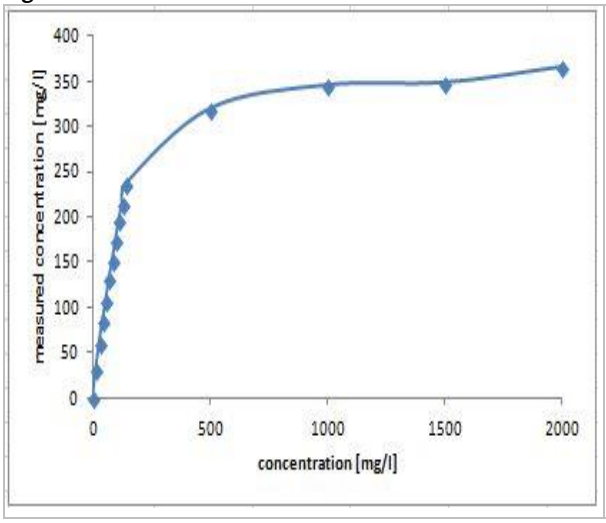
3.7 Prozone Effect

The prozone effect of CRP on AU 400 was checked by employing a high concentrated pool serum on AU 400. Result means were calculated from 3-fold determinations.

Material

Reagent	**Manufacturer**	**REF**	**LOT**
CRP	HUMAN	11241	0049/0046
CRP Standard	HUMAN	11341	16005
Sample	Pool serum, LOT PRO10078		

Figure



No prozone effect upto 2000 mg/l

Conclusion

No prozone effect could be observed up to 2000 mg/l.

4 Recovery of Control sera

A number of commercially available control sera were employed. The control sera were reconstituted/prepared according to the manufacturer's instructions. The mean value was calculated and compared with the target mean of the respective control sera.

4.1 Recovery of Control sera – multi-point calibration – CRP kit

Criteria

Check	**Acceptance criteria**
Recovery	within range
Deviation result mean from target mean	≤ 10%

Used Material

Analyzer	**Manufacturer**	**REF**	
AU 400	Beckman Coulter	N1254600	
Reagent	**Manufacturer**	**REF**	**LOT**
CRP	HUMAN	11241	0001
CRP Standard	HUMAN	11341	16005
Sample	HUMAN's and commercial controls (Beckman Coulter, Bio-Rad, INVICON)		

Results

Control recovery				multi-point calibration	
Name	**LOT**	**Target mg/l**	**Range mg/l**	**Result mg/l**	**Within range YES/NO**
TURBIDOS L1	H022	8.6	6.9 – 10.3	9.8	YES
TURBIDOS L2	H022	60.6	48.5 – 72.7	61.5	YES
Immunology Control L1	0034	15.1	12.1 – 18.1	14.1	YES
Immunology Control L2	0038	25.6	20.5 – 30.8	22.7	YES
Seronorm L1	1311546	8.5	7.3 – 9.6	8.7	YES
Seronorm L2	1311547	102.0	89.0 – 116	97.4	YES
Liquicheck Immunology L1	66321	6.3	<5.0– 8.7	6.5	YES
Liquicheck Immunology L2	66322	25.6	20.6 – 30.6	24.2	YES
					Dev.%
Mean		**31.5**		**30.6**	**-2.9**

4.2 Recovery of Control sera – multi-point calibration – CRP kit and CRP buffer kit

Criteria

Check	**Acceptance criteria**
Recovery	within range
Deviation result mean from target mean	≤ 10%

Used Material

Analyzer	**Manufacturer**	**REF**	
HumaStar 600	HUMAN	16660	
Reagent	**Manufacturer**	**REF**	**LOT**
CRP antiserum	HUMAN	11241	0053; 0054
CRP buffer	HUMAN	11141	CEN081
CRP standard	HUMAN	11341	17003
Sample	HUMAN's and commercial controls (Beckman Coulter, Bio-Rad)		

Results

Control recovery for CRP antiserum, LOT 0053, CRP buffer LOT CEN081				multi-point calibration	
Name	**LOT**	**Target mg/l**	**Range mg/l**	**Result mg/l**	**Within range YES/NO**
Liquicheck Immunology L1	66341	6.29	<5.0 – 8.5	5.55	YES
Liquicheck Immunology L2	66342	24.2	19.4 – 28.9	24.2	YES
Liquicheck Immunology L3	66343	46.2	37.2 – 55.2	43.8	YES
Immunology Control L1	0037	13.3	10.6 – 15.9	11.6	YES
Immunology Control L2	0038	25.6	20.5 – 30.8	24.1	YES
TURBIDOS L1	H023	5.66	< 5.0 – 6.79	5.90	YES
TURBIDOS L2	H023	57.9	46.3 – 69.5	57.9	YES
					Dev.%
Mean		**25.6**		**24.7**	**-3.5**

Control recovery for CRP antiserum, LOT 0054, CRP buffer LOT CEN081				CRP – multi-point calibration	
Name	**LOT**	**Target mg/l**	**Range mg/l**	**Result mg/l**	**Within range YES/NO**
Liquicheck Immunology L1	66341	6.29	<5.0– 8.5	6.15	YES
Liquicheck Immunology L2	66342	24.2	19.4 – 28.9	24.5	YES
Liquicheck Immunology L3	66343	46.2	37.2 – 55.2	44.4	YES
Immunology Control L1	0037	13.3	10.6 – 15.9	11.7	YES
Immunology Control L2	0038	25.6	20.5 – 30.8	23.5	YES
TURBIDOS L1	H023	5.66	<5.0 – 6.79	5.95	YES
TURBIDOS L2	H023	57.9	46.3 – 69.5	58.5	YES
					Dev.%
Mean		**25.6**		**25.0**	**-2.5**

Conclusion

Control findings for CRP kit, REF 11241, and CRP kit, REF 11241, combined with CRP buffer kit, REF 11141, met acceptance criteria. CRP multipurpose reagents show a good recovery of control sera in the multi-point calibration.

4.3 Recovery of Control sera – 1-point calibration – CRP kit

Criteria

Check	**Acceptance criteria**
Recovery	within range
Deviation result mean from target value	≤ 10%

Used Material

Analyzer	**Manufacturer**	**REF**	
AU 400	Beckman Coulter	N1254600	
Reagent	**Manufacturer**	**REF**	**LOT**
CRP	HUMAN	11241	0001
CRP Standard	HUMAN	11341	16005
Sample	HUMAN's and commercial controls (Beckman Coulter, Bio-Rad, INVICON)		

Results

Control recovery				1-point calibration	
Name	**LOT**	**Target mg/l**	**Range mg/l**	**Result mg/l**	**Within range YES/NO**
TURBIDOS L1	H022	8.6	6.9 – 10.3	10.2	YES
TURBIDOS L2	H022	60.6	48.5 – 72.7	68.7	YES
Immunology Control L1	0034	15.1	12.1 – 18.1	15.7	YES
Immunology Control L2	0038	25.6	20.5 – 30.8	27.9	YES
Seronorm L1	1311546	8.5	7.3 – 9.6	8.8	YES
Seronorm L2	1311547	102	89.0 – 116	102	YES
Liquicheck Immunology L1	66321	6.3	<5.0 – 8.7	5.8	YES
Liquicheck Immunology L2	66322	25.6	20.6 – 30.6	29.0	YES
					Dev.%
Mean		**31.5**		**33.5**	**6.3**

4.4 Recovery of Control sera – 1-point calibration – CRP kit and CRP buffer kit

Criteria

Check	Acceptance criteria
Recovery	within range
Deviation result mean from target value	≤ 10%

Used Material

Analyzer	Manufacturer	REF	
AU 480	Beckman Coulter	N3660400	
Reagent	**Manufacturer**	**REF**	**LOT**
CRP antiserum	HUMAN	11241	0053; 0054
CRP buffer	HUMAN	11141	CEN081
CRP Standard	HUMAN	11341	17003
Sample	HUMAN's and commercial controls (Beckman Coulter, Bio-Rad)		

Results

Control recovery for CRP antiserum, LOT 0053, CRP buffer LOT CEN081				1-point calibration	
Name	**LOT**	**Target mg/l**	**Range mg/l**	**Result mg/l**	**Within range YES/NO**
Liquicheck Immunology L1	66341	6.29	<5.0 – 8.5	5.28	YES
Liquicheck Immunology L2	66342	24.2	19.4 – 28.9	24.7	YES
Liquicheck Immunology L3	66343	46.2	37.2 – 55.2	43.4	YES
Immunology Control L1	0037	13.3	10.6 – 15.9	11.8	YES
Immunology Control L2	0038	25.6	20.5 – 30.8	24.3	YES
TURBIDOS L1	H023	5.66	<5.0 – 6.79	5.19	YES
TURBIDOS L2	H023	57.9	46.3 – 69.5	56.8	YES
					Dev.%
Mean		**26.3**		**24.5**	**-6.8**

Control recovery for CRP antiserum, LOT 0054, CRP buffer LOT CEN081				1-point calibration	
Name	**LOT**	**Target mg/l**	**Range mg/l**	**Result mg/l**	**Within range YES/NO**
Liquicheck Immunology L1	66341	6.29	<5.0 – 8.5	6.08	YES
Liquicheck Immunology L2	66342	24.2	19.4 – 28.9	25.2	YES
Liquicheck Immunology L3	66343	46.2	37.2 – 55.2	44.6	YES
Immunology Control L1	0037	13.3	10.6 – 15.9	12.5	YES
Immunology Control L2	0038	25.6	20.5 – 30.8	24.9	YES
TURBIDOS L1	H023	5.66	<5.0 – 6.79	5.87	YES
TURBIDOS L2	H023	57.9	46.3 – 69.5	58.2	YES
					Dev.%
Mean		**26.3**		**25.3**	**-3.6**

Conclusion

Control findings for CRP kit, REF 11241, and CRP kit, REF 11241, combined with CRP buffer kit, REF 11141, met acceptance criteria. CRP multipurpose reagents show a good recovery of control sera in the 1-point calibration.

5 Method Comparison

5.1 Method comparison – multi-point calibration

CRP on AU 480, Beckman Coulter (test) was compared with CRP, Beckman Coulter, on AU 480, Beckman Coulter (reference). Patient samples as well as control sera (n = 52) were employed in the comparison. The results were evaluated by a non-parametric regression analysis according to Passing & Bablok.

Criteria

Passing & Bablok	**Acceptance criteria**
Slope	0.95 – 1.05
Correlation coefficient	r > 0.95

Used Material

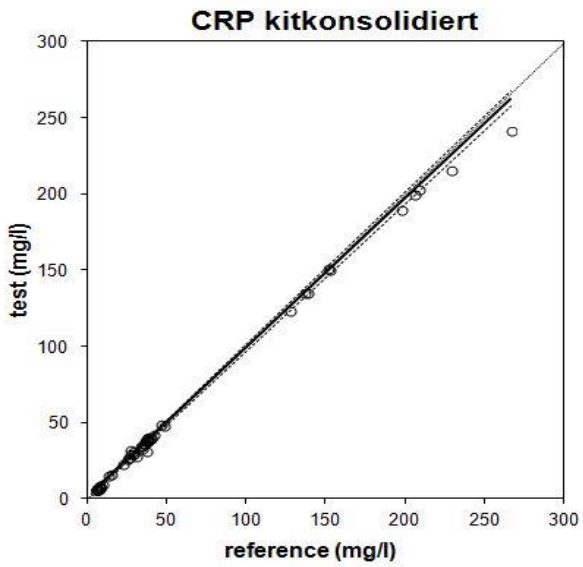
Reagent	**Manufacturer**	**REF**	**LOT**
CRP (test)	HUMAN	11241	0001
CRP (reference)	Beckman Coulter	OSR6147	9451
CRP Standard (test)	HUMAN	11341	n/a
Serum protein multi-calibrator (reference)	Beckman Coulter	ODR3021	n/a
Sample	Patient samples and various controls		

Results

Sample-no.	**Unit**	**Mean Reference AU 480**	**Mean Test AU 480**	**Difference**
1	mg/l	8.10	8.39	0.29
2	mg/l	8.05	7.15	-0.90
3	mg/l	5.56	5.75	0.19
4	mg/l	5.99	6.37	0.39
5	mg/l	38.4	40.4	2.0
6	mg/l	36.1	36.4	0.3
7	mg/l	37.0	31.2	-5.7
8	mg/l	35.7	36.7	1.0
9	mg/l	37.9	40.2	2.3
10	mg/l	37.8	39.9	2.1
11	mg/l	26.5	27.3	0.9
12	mg/l	36.3	37.8	1.5
13	mg/l	27.0	32.3	5.3
14	mg/l	29.2	31.1	1.8
15	mg/l	30.9	28.0	-2.9
16	mg/l	27.1	29.7	2.5
17	mg/l	25.7	26.6	0.9
18	mg/l	33.6	34.4	0.8
19	mg/l	15.0	16.6	1.6
20	mg/l	29.3	29.6	0.3
21	mg/l	13.8	15.6	1.8
22	mg/l	46.7	49.0	2.3
23	mg/l	41.5	42.3	0.8
24	mg/l	137	135	-1
25	mg/l	138	135	-3
26	mg/l	209	203	-5
27	mg/l	229	216	-13
28	mg/l	266	241	-25
29	mg/l	152	152	0
30	mg/l	128	123	-4

31	mg/l	198	190	-8
32	mg/l	205	200	-6
33	mg/l	152	150	-2
34	mg/l	40.4	40.5	0.1
35	mg/l	48.3	48.1	-0.1
36	mg/l	38.4	39.2	0.8
37	mg/l	34.2	35.0	0.8
38	mg/l	26.1	27.1	1.0
39	mg/l	28.7	29.4	0.7
40	mg/l	40.1	39.6	-0.4
41	mg/l	22.7	23.4	0.7
42	mg/l	38.0	38.0	0.0
43	mg/l	34.4	32.9	-1.4
44	mg/l	7.86	7.87	0.01
45	mg/l	5.21	3.19	-2.02
46	mg/l	6.08	6.06	-0.02
47	mg/l	6.43	6.54	0.11
48	mg/l	5.92	7.38	1.47
49	mg/l	6.62	6.45	-0.17
50	mg/l	6.55	6.70	0.15
51	mg/l	8.28	8.66	0.38
52	mg/l	9.41	9.90	0.49
53	mg/l	7.54	7.51	-0.03
Mean	**mg/l**	**55.1**	**54.2**	
Min	**mg/l**	**5.56**	**5.75**	
Max	**mg/l**	**266**	**241**	

Figure



Y = 0.983 X + 0.741 (mg/l)
r = 0.999
Y = test
X = reference

Conclusion

CRP multipurpose reagent, HUMAN, on AU 480, Beckman Coulter, correlates significantly with CRP, Beckman Coulter, on AU 480, Beckman Coulter (r = 0.999), and no significant deviation could be observed with any specific sample:

Y = 0.983 X+ 0.741 (mg/l)

Y = test, X = reference

5.2 Method comparison – 1-point calibration

CRP on AU 480, Beckman Coulter (test) was compared against CRP, Beckman Coulter, on AU 480, Beckman Coulter (reference). Patient samples as well as control sera (n = 53) were used in the comparison. The results were evaluated by a non-parametric regression analysis according to Passing & Bablok.

Criteria

Passing & Bablok	**Acceptance criteria**
Slope	0.95 – 1.05
Correlation coefficient	r > 0.95

Used Material

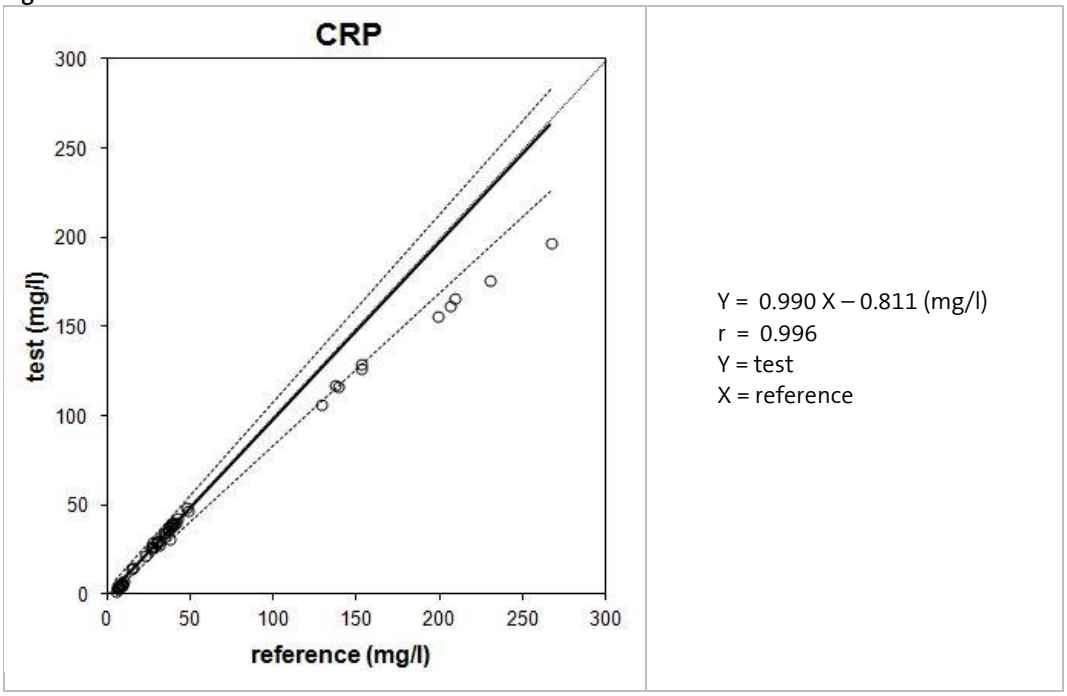
Reagent	**Manufacturer**	**REF**	**LOT**
CRP (test)	HUMAN	11241	0001
CRP (reference)	Beckman Coulter	OSR6147	9451
CRP Standard (test)	HUMAN	11341	n/a
Serum protein multi-calibrator (reference)	Beckman Coulter	ODR3021	n/a
Sample	Patient samples and various controls		

Results

Sample-no.	**Unit**	**Mean Reference AU 480**	**Mean Test AU 480**	**Difference**
1	mg/l	8.10	6.32	-1.78
2	mg/l	8.05	5.11	-2.95
3	mg/l	5.56	3.77	-1.80
4	mg/l	5.99	4.13	-1.86
5	mg/l	38.4	40.2	1.83
6	mg/l	36.1	36.1	0.00
7	mg/l	37,0	31.2	-5.79
8	mg/l	35.7	36.6	0.93
9	mg/l	37.9	39.7	1.80
10	mg/l	37.8	39.3	1.57
11	mg/l	26.5	27.0	0.49
12	mg/l	36.3	38.0	1.75
13	mg/l	27.0	26.9	-0.06
14	mg/l	29.2	30.1	0.83
15	mg/l	30.9	27.7	-3.24
16	mg/l	27.1	29.3	2.14
17	mg/l	25.7	26.1	0.44
18	mg/l	33.6	34.2	0.66
19	mg/l	15.0	15.2	0.19
20	mg/l	29.3	29.8	0.51
21	mg/l	13.8	14.5	0.72
22	mg/l	46.7	48.6	1.94
23	mg/l	41.5	42.7	1.26
24	mg/l	137	117	-19.09
25	mg/l	138	117	-21.76
26	mg/l	209	166	-42.81
27	mg/l	229	176	-53.03
28	mg/l	266	197	-69.61
29	mg/l	152	129	-23.05
30	mg/l	128	107	-20.86
31	mg/l	198	1566	-41.38
32	mg/l	205	162	-43.22

33	mg/l	152	127	-25.61
34	mg/l	40.4	40.5	0.05
35	mg/l	48.3	47.0	-1.28
36	mg/l	38.4	39.5	1.05
37	mg/l	34.2	35.0	0.82
38	mg/l	26.1	26.3	0.16
39	mg/l	28.7	28.4	-0.23
40	mg/l	40.1	39.3	-0.78
41	mg/l	22.7	22.4	-0.28
42	mg/l	38.0	37.7	-0.31
43	mg/l	34.4	32.7	-1.68
44	mg/l	7.86	6.07	-1.80
45	mg/l	5.21	1.79	-3.42
46	mg/l	6.08	3.94	-2.14
47	mg/l	6.43	4.14	-2.29
48	mg/l	5.92	5.53	-0.39
49	mg/l	6.62	4.56	-2.06
50	mg/l	6.55	4.72	-1.83
51	mg/l	8.28	6.78	-1.50
52	mg/l	9.41	7.43	-1.98
53	mg/l	7.54	5.54	-2.00
Mean	**mg/l**	**54.1**	**46.9**	
Min	**mg/l**	**5.21**	**1.79**	
Max	**mg/l**	**266**	**197**	

Figure



Y = 0.990 X – 0.811 (mg/l)
r = 0.996
Y = test
X = reference

Conclusion

CRP multipurpose reagent on AU 480, Beckman Coulter, correlates siginificantly with CRP, Beckman Coulter, on AU 480, Beckman Coulter (r = 0.996), and no significant deviation could be observed with any specific sample:
Y = 0.990 X – 0.811 (mg/l)
Y = test, X = reference

6 Real-Time Stability

The C-REACTIVE PROTEIN (CRP) multipurpose reagent (REF 11241) was stored at 2...8°C. The performance was tested at several storage times, covering a range from 0% to 125% of the shelf life (18 months at 2...8°C). The real-time stability was checked with a control recovery test and a linearity test.

6.1 Recovery of Control sera- CRP Reagent

The C-REACTIVE PROTEIN (CRP) multipurpose reagent was used for a quantitiative CRP detection with HUMAN control sera and commercially available control sera. Tests were run in duplicate (n=2), with 3 different reagent LOTs on an AU 400 or AU 480 analyzer (1-point-calibration). The mean values of test results with fresh reagent (=reference) and stored reagent were put into comparison.

Criteria

Check	**Acceptance criteria**
Recovery	within range
Deviation result mean from reference mean	≤ 10%

Material

Reagent	**Manufacturer**	**REF**	**LOT**
C-REACTIVE PROTEIN (CRP)	HUMAN	11241	15003, 15004, 15006
CRP Standard	HUMAN	11341	14005
Sample	HUMAN control sera, other control sera (Beckman, BioRad, Invicon)		

Results

LOT 15003							
				Reference		**0 months 2-8°C**	
Name	**LOT**	**Target mg/l**	**Range mg/l**	**Result mg/l**	**Within range YES/NO**	**Result mg/l**	**Within range YES/NO**
Liquicheck IM1	66301	7.21	5.03 - 9.39	9.33	YES	10.1	NO
Liquicheck IM2	66302	27.3	21.9 - 32.7	34.7	NO	35.9	NO
Liquicheck IM3	66303	53.6	44.1 - 63.0	58.0	YES	59.3	YES
TURBIDOS 1	H021	12.9	10.3 - 15.0	11.9	YES	12.6	YES
TURBIDOS 2	H021	81.1	64.9 - 97.3	79.8	YES	80.7	YES
ITA 1	0031	13.7	11.0 - 16.4	17.4	NO	18.3	NO
ITA 2	0032	28.5	22.8 - 34.2	33.7	YES	34.6	NO
							Dev.%
Mean		**32.0**		**35.0**		**35.9**	**4.1**

The control recovery data of the in-house control sera were all within range. The control recovery data of control sera of other brands showed a good conformity between reference and real time stability (≤ 10%) and were therefore accepted.

LOT 15003							
				Reference		18 months 2-8°C	
Name	**LOT**	**Target mg/l**	**Range mg/l**	**Result mg/l**	**Within range YES/NO**	**Result mg/l**	**Within range YES/NO**
Seronorm 1	1311546	8.45	7.31 - 9.59	6.98	NO	5.18	NO
Seronorm 2	1311547	102	89.0 - 116	82.0	NO	76.2	NO
TURBIDOS 1	H022	13.6	10.9 - 16.3	12.3	YES	11.9	YES
TURBIDOS 2	H022	78.3	62.6 - 94.0	67.7	YES	67.3	YES
ITA 1	0034	15.0	12.1 - 18.1	16.9	YES	17.0	YES
ITA 2	0038	25.6	20.5 - 30.8	28.6	YES	28.3	YES
							Dev.%
Mean		**40.5**		**35.7**		**34.3**	**-6.2**

The Seronorm controls are not well suited for the system. All other controls are within the range. The control recovery data showed a good conformity between reference and real time stability (≤ 10%) and were accepted.

LOT 15004							
				Reference		1 month 2-8°C	
Name	**LOT**	**Target mg/l**	**Range mg/l**	**Result mg/l**	**Within range YES/NO**	**Result mg/l**	**Within range YES/NO**
Liquicheck IM 1	66301	7.21	5.03 - 9.39	8.60	YES	8.57	YES
Liquicheck IM 2	66302	27.3	21.9 - 32.7	31.4	YES	30.9	YES
Liquicheck IM 3	66303	53.6	44.1 - 63.0	52.3	YES	52.4	YES
Turbidos 1	H021	12.9	10.3 - 15.5	10.8	YES	11.1	YES
Turbidos 2	H021	81.1	64.9 - 97.3	71.9	YES	72.5	YES
ITA 1	0034	15.0	12.1 - 18.1	16.7	YES	17.2	YES
ITA 2	0035	28.9	23.1 - 34.7	31.8	YES	32.6	YES
							Dev.%
Mean		**32.3**		**31.9**		**32.2**	**1.0**

LOT 15004							
				Reference		18 months 2-8°C	
Name	**LOT**	**Target mg/l**	**Range mg/l**	**Result mg/l**	**Within range YES/NO**	**Result mg/l**	**Within range YES/NO**
Liquicheck IM 1	66341	6.29	5.00 - 8.50	8.01	YES	8.96	NO
Liquicheck IM 2	66342	24.2	19.4 - 28.9	31.8	NO	33.4	NO
Liquicheck IM 3	66343	46.2	37.2 - 55.2	52.0	YES	53.5	YES
Turbidos 1	H022	13.6	10.9 - 16.3	13.0	YES	13.7	YES
Turbidos 2	H022	78.3	62.6 - 94.0	72.4	YES	75.2	YES
ITA 1	0034	15.0	12.1 - 18.1	17.5	YES	18.0	YES
ITA 2	0038	25.6	20.5 - 30.8	30.0	YES	30.8	YES
							Dev.%
Mean		**29.9**		**32.1**		**33.4**	**5.0**

The control recovery data of the in-house control sera and most of the external controlsera were within range. The control recovery data of control sera showed – with one exception - a good conformity between reference and real time stability (≤ 10%) and were therefore accepted.

LOT 15006							
				Reference		3.5 months 2-8°C	
Name	**LOT**	**Target mg/l**	**Range mg/l**	**Result mg/l**	**Within range YES/NO**	**Result mg/l**	**Within range YES/NO**
Liquicheck IM1	66321	6.27	5.00 - 8.66	8.94	NO	8.90	NO
Liquicheck IM2	66322	25.6	20.0 - 30.6	34.2	NO	34.1	NO
Liquicheck IM3	66323	47.1	38.2 - 56.0	54.4	YES	53.8	YES
Turbidos 1	H021	12.9	10.3 - 15.5	12.3	YES	12.4	YES
Turbidos 2	H021	81.1	64.9- 97.3	81.2	YES	80.4	YES
ITA 1	0034	13.7	11.0 - 16.4	19.4	NO	19.2	NO
ITA 2	0035	28.5	22.8 - 34.2	36.1	NO	36.5	NO
							Dev.%
Mean		30.7		35.2		35.0	-0.2

The control recovery data of the in-house control sera were all within range. The control recovery data of control sera of other brands showed a good conformity between reference and real time stability (≤ 10%) and were therefore accepted.

LOT 15006							
				Reference		18 months 2-8°C	
Name	**LOT**	**Target mg/l**	**Range mg/l**	**Result mg/l**	**Within range YES/NO**	**Result mg/l**	**Within range YES/NO**
Turbidos 1	H022	13.6	10.9 - 16.3	11.7	YES	12.6	YES
Turbidos 2	H022	78.3	62.6 - 94.0	69.2	YES	71.4	YES
ITA 1	0037	13.3	10.6 - 15.9	14.7	YES	16.5	NO
ITA 2	0038	25.6	20.5 - 30.8	29.0	YES	30.6	YES
Liquicheck IM 1	66341	6.29	5.00 - 8.50	7.75	YES	8.68	NO
Liquicheck IM 2	66342	24.2	19.4 - 28.9	29.3	NO	30.9	NO
Liquicheck IM 3	66343	46.2	37.2 - 55.2	49.9	YES	52.1	YES
							Dev.%
Mean		26.9		26.9		28.4	**7.2**

Some of the controls of other brands does not comply with the specification. The mean deviation as well as the recovery of the inhouse controls are within range. For these reason, the data were accepted.

The Control recovery data was within range, with some outliers, which were mainly due to the use of control sera of other brands. The control recovery data of the in-house control sera were all within range. Therefore the data were accepted. The deviation between reference batches and the real-time batch was all the time ≤ 10%, and this acceptance criterion was met.

Conclusion: The control recovery data proves a shelf life of C-REACTIVE PROTEIN (CRP) multipurpose reagent (REF 11241) of 18 months at 2...8°C.

6.2 Linearity

Linearity was tested with a dilution series of a high-concentration pool serum. The analytical results and the calculated results (linear regression) were compared. The test is calibrated with a standard serum, and the linear range depends on the LOT-specific calibration. Tests were run with 3 different reagent LOTs, on an AU480 or AU 400 analyzer.

Criteria

Linearity	Acceptance criteria
Deviation from regression line	≤ 10%

Outliers are marked in grey

Material

Reagent	Manufacturer	REF	LOT
C-REACTIVE PROTEIN (CRP)	HUMAN	12006	15003, 15004, 15006
CRP Standard	HUMAN	11341	14005
Sample	Dilution series (1:10) of pool serum with saline 0.9%		

Results

LOT 15003, 0 months/ 2...8°C				
High Pool Content	**Analytical Data**	**Regressed Data**	**Deviation from Regression Line**	
(%)	**mg/l**	**mg/l**	**mg/l**	**(%)**
0	-0.21	14.4	-14.6	
10	36.0	36.5	-0.5	-1.4
20	64.4	58.5	5.8	9.9
30	87.9	80.6	7.3	9.1
40	110	103	7	7.1
50	131	125	7	5.4
60	148	147	1	1.0
70	166	169	-3	-1.7
80	180	191	-10	-5.5
90	195	213	-18	-8.5
100	212	235	-23	-10.0

LOT 15003, 18 months/ 2...8°C				
High Pool Content	**Analytical Data**	**Regressed Data**	**Deviation from Regression Line**	
(%)	**mg/l**	**mg/l**	**mg/l**	**(%)**
0	-1.31	18.7	-20.3	
10	38.7	41.1	-2.3	-5.5
20	69.1	63.5	6.0	9.4
30	96.2	85.9	10.2	11.8
40	119	108	10.6	9.8
50	140	131	9	7.1
60	158	153	5	3.1
70	174	175	-1	-0.7
80	194	198	-4	-2.0
90	207	220	-13	-5.9
100	222	243	-21	-8.6

The deviation of one point is accepted in case of the real time stability of the batch 15003 after 18 months.

LOT 15004, 0 months/ 2...8°C				
High Pool Content	**Analytical Data**	**Regressed Data**	**Deviation from Regression Line**	
(%)	**mg/l**	**mg/l**	**mg/l**	**(%)**
0	-0.18	14.1	-14.2	
10	31.6	33.0	-1.4	-4.3
20	56.4	52.0	4.4	8.4
30	77.9	71.0	6. 9	9.7
40	96.7	90.0	6.7	7.4
50	115	109	6.	6.0
60	131	128	3	2.4

70	146	147	-1	-0.3
80	166	166	-0	-0.1
90	174	185	-11	-6.0
100	188	204	-16	-7.8

LOT 15004, 18 months/ 2...8°C				
High Pool Content	**Analytical Data**	**Regressed Data**	**Deviation from Regression Line**	
(%)	**mg/l**	**mg/l**	**mg/l**	**(%)**
0	-1.38	12.1	-13.5	
10	42.3	39.4	2.9	7.4
20	72.4	66.6	5.8	8.8
30	101	93.8	7.5	8.0
40	127	121	6	4.9
50	149	148	1	0.7
60	173	176	-2	-1.3
70	195	203	-8	-3.7
80	210	230	-20	-8.6
90	232	257	-25	-9.8
100	242	285	-42	-14.8

The real time linearity of the batch 15004 after 18 months is linear up to 230 mg/l.

LOT 15006, 3.5 months/ 2...8°C				
High Pool Content	**Analytical Data**	**Regressed Data**	**Deviation from Regression Line**	
(%)	**mg/l**	**mg/l**	**mg/l**	**(%)**
0	-0.20	14.7	-14.9	
10	43.7	41.9	1.8	4.4
20	75.6	69.0	6.6	9.5
30	105	96.2	9.2	9.6
40	131	123	7	5.9
50	153	150	3	1.9
60	174	178	-4	-2.3
70	196	205	-9	-4.3
80	216	232	-16	-7.0
90	222	259	-37	-14.3
100	244	286	-42	-14.7

The real time linearity of the batch 15006 after 3.5 months is linear up to 215 mg/l.

LOT 15006, 18 months/ 2…8°C				
High Pool Content	**Analytical Data**	**Regressed Data**	**Deviation from Regression Line**	
(%)	**mg/l**	**mg/l**	**mg/l**	**(%)**
0	-0.43	13.0	-13.4	
10	43.8	42.0	1.8	4.2
20	77.8	71.0	6.8	9.6
30	108	100	8	7.9
40	135	129	6	4.9
50	161	158	23	1.8
60	184	187	-3	-1.7
70	201	216	-15	-7.1
80	221	245	-24	-9.8
90	237	274	-37	-13.3
100	249	303	-54	-18.0

The real time linearity of the batch 15006 after 18 months is linear up to 220 mg/l.
The linearity data met acceptance criteria, with a deviation of one outliers. The linear range of about 0 mg/l to 190 mg/l was confirmed for a shelf life of 18 months at 2…8°C.

Conclusion: The real-time stability data proves a shelf life of C-REACTIVE PROTEIN (CRP) multipurpose reagent (REF 11241) of 18 months at 2…8°C.

6.3 Recovery of control sera – CRP Standard

Different LOTs of CRP Standard were used in this study. The mean values of measurements with fresh CRP standard and 2 different LOTs of CRP standards were calculated and compared with the target values of the respective CRP Standard.

Criteria

Check	**Acceptance criteria**
Recovery	within range
Deviation result mean from target value	≤ 10%

Reagent	**Manufacturer**	**REF**	**LOT**
CRP Standard	HUMAN	11341	H013/reference
CRP Standard	HUMAN	11341	H011/19 months at 2…8°C
CRP Standard	HUMAN	11341	H010/20 months at 2…8°C

Results

CRP Standard recovery			**CRP reagent LOT H010**		**CRP reagent LOT H016**		**CRP reagent LOT 031027GC57**	
Name	**LOT**	**Target**	**Result**	**Dev.**	**Result**	**Dev.**	**Result**	**Dev.**
		mg/l	**mg/l**	**%**	**mg/l**	**%**	**mg/l**	**%**
CRP Standard	H013/ reference	170	171	**0.6**	170	**0**	170	**0**
CRP Standard	H011/ 19 months	170	169	**-0.6**	170	**0**	168	**-1.2**
CRP Standard	H010/ 20 months	170	172	**1.2**	168	**-1.18**	168	**-1.2**

Conclusion
The CRP Standard recovery met the acceptance criteria (deviation result mean from target value), confirming the stability of the product. Real-time stability data for CRP Standard confirm a shelf life of 18 months at 2...8°C.

7 Open-Vial Stability

7.1 Recovery of control sera – CRP Reagent

The recovery of control sera of CRP was checked according to the procedure already described in section 4 on AU 480. For testing the open-vial stability the CRP reagents were stored at 2...8°C after opening for 61 days.

Criteria

Check	Acceptance criteria
Recovery	within range
Deviation result mean from fresh mean	≤ 10%

Used Material

Reagent	Manufacturer	REF	LOT
CRP	HUMAN	11241	R1 0040, R2 0037
CRP Standard	HUMAN	11341	15002
Sample	HUMAN's and commercial controls (Beckman Coulter)		

Results

Control recovery				CRP		
				Fresh	61 days after opening	
Name	LOT	Target mg/l	Range mg/l	Result mg/l	Result mg/l	Within range YES/NO
Immunology control serum L1	0034	15.1	12.0 – 28.0	8.6*	9.3*	NO
Immunology control serum L2	0035	28.9	23.6 – 35.5	26.6	27.2	YES
TURBIDOS L2	H021	72.3	57.6 - 86.4	76.1	72.7	YES
						Dev.%
Mean						**-1.9**

*out of control range; not excluded because the result for deviation to fresh is rated higher in this study.

Conclusion
The control findings for CRP multipurpose reagent met acceptance criteria (deviation to fresh mean). The open-vial stability of the CRP reagent is confirmed for at least 60 days 2...8°C after opening.

7.2 Recovery of CRP Standard

The CRP standard was diluted in 4 steps, incubated at 2...8°C, and tested with CRP reagent, following the Standard Operating Procedures for Open Vial Stability.

Criteria

Check	Acceptance criteria
Difference of result to target value	≤ 10%

Standard Dilutions	Incubation Times	Analyzer	CRP Reagent
REF 11341	2...8°C	HumaStar	REF 11241600
25%, 50%, 75%, 100%	0 to 49 days	HS 600 (7)	LOT 20005

CRP Standard	0d	7d	14d	21d	35d	42d	49d
25%	100	104	104	97	98	97	103
50%	100	101	105	97	99	98	99
75%	100	100	110	101	101	101	102
100%	100	101	106	102	101	101	103

Conclusion
The data met acceptance criteria.
The CRP Standard (REF 11341) has an open-vial stability of > 48 days (6 weeks) at 2...8°C.

8 Interferences

8.1 Interferences

Interference by bilirubin, hemoglobin, trglycerides and anticoagulants (fluoride, heparin, EDTA, citrate) of CRP reagent was tested by adding known amounts of the potentially interfering substance to a known sample. Recoveries were analysed according to the method of Glick et al. (Clin.Chem. 1986. 32 470-5).

Criteria

Glick	Acceptance criteria
Glick number	≤ 2
Recovery spiked samples vs unspiked sample	90 – 110%

Used Material

Reagent	Manufacturer	REF	LOT
CRP	HUMAN	11241	n/a
CRP Standard	HUMAN	11544	n/a
Samples	Samples spiked with interfering substance		

Results

Bilirubin		Hemoglobin		Triglyceride	
Conc.	Analytical Result	Conc.	Analytical Result	Conc.	Analytical Result
mg/dl	%	mg/dl	%	mg/dl	%
0	100	0	100	0	100
4	101.6	50	100.3	250	99.6
8	101	100	99.2	500	99.4
12	100.1	150	99.4	750	99.6
16	100	200	98.3	1000	99.4
20	100.4	250	97.8	1250	100.1
24	98.6	300	98.5	1500	99.7
28	97.8	350	98.5	1750	99.6
32	98.6	400	98.7	2000	99.5
36	99.4	450	97.6	2250	99.7
40	98.3	500	97.2	2500	99.7
Glick	**1**		**1**		**1**

Citrate		EDTA		Fluoride		Heparin	
Conc.	Analytical Result	Conc.	Analytical Result	Conc.	Analytical Result	Conc.	Analytical Result
mg/ml	%	mg/ml	%	mg/ml	%	Units/ml	%
0	100	0	100	0	100	0	100
2.5	98.8	0.5	101.4	0.8	100.3	2.5	99.8
5.0	99.6	1.0	102.6	1.6	100.6	5.0	100
7.5	100.0	1.5	102.4	2.4	102.2	7.5	99.6
10.0	100.6	2.0	102.2	3.2	101.6	10.0	99.4
12.5	100.3	2.5	100.0	4.0	102.1	12.5	99.7
15.0	100.0	3.0	102.4	4.8	101.7	15.0	99.1
17.5	100.6	3.5	101.8	5.6	101.7	17.5	99.7
20.0	100.8	4.0	101.2	6.4	101.2	20.0	99.1
22.5	101.2	4.5	102.4	7.2	102.3	22.5	98.9
25.0	100.6	5.0	102.0	8.0	102	25.0	99.4
Glick	**1**		**1**		**1**		**1**

Conclusion

No interference of CRP multipurpose reagent was detected up to following concentrations:

Interfering substance	CRP on AU 400
Bilirubin	up to 40 mg/dl
Hemoglobin	up to 500 mg/dl
Triglycerides	up to 2500 mg/dl
Citrat	upto 25.0 mg/ml
EDTA	upto 5.0 mg/ml
Fluoride	upto 8.0 mg/ml
Heparin	upto 25.0 Units/ml

9 Traceability

CRP multipurpose reagent, REF 11241 is calibrated with CRP standard, REF 11341. CRP standard is traceable to the international reference material ERM-DA472/IFCC.