

# Design Verification

SERODOS® and SERODOS® plus



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## 1 Value Adjustment

The liquid raw material is tested for the content of each individual parameter. If necessary, respective parameters are spiked or stripped to meet the specification for normal, elevated, or pathological range.

The values for each parameter are checked again after lyophilisation. If all parameters comply with the specifications, the target value assignment is started.

## 2 Target Determination

The target value determination of HUMAN's SERODOS® control sera is performed by own QC laboratories and external laboratories employing different methods and instruments. The assigned target values for each parameter reflect the consensus values, obtained by statistical evaluation of the results of all participating laboratories.

## 3 Stability

The shelf life of SERODOS® and SERODOS® plus has been confirmed by the results of real-time studies. Each LOT of control serum is checked by temperature stress studies at the time of production. Retained samples of each batch are further tested at suitable intervals to monitor real-time stability during the assigned shelf life.

### SERODOS® and SERODOS® plus

Lyophilized SERODOS® and SERODOS® plus controls have an assigned shelf of 4 years from the date of production when stored at 2-8°C.

Reconstituted SERODOS® and SERODOS® plus remain stable for 7 days at 2...8 °C and for 1 month at -20 °C. However, some constituents may change their concentration within earlier periods (e.g. glucose, bilirubin, GOT, GPT). For these constituents refer to section 3.2 to 3.4, where LOT-specific deviations are listed.

### 3.1 Real-Time Stability

Below typical stability data on some constituents are summarized. The data compare results obtained from real-time storage (2...8°C) and deep-frozen storage (-80°C).

#### Results

SERODOS®		Fresh	Check dates					
Raw material LOT 243UN		2000-07	2002-08			2004-07		
Parameter	Unit	Target	4°C	-80°C	% DEV	4°C	-80°C	% DEV
Albumin	g/l	42.2	44.8	45.3	6.2%	43.5	43.5	3.1%
Alk. Phosphatase	U/l	295	342	350	15.9%	307	306	4.1%
GPT (ALT)	U/l	54	60	56	11.1%	49	52	-9.3%
alpha-Amylase	U/l	97	104	106	7.2%	123	127	26.8%
GOT (AST)	U/l	55	61	61	10.9%	54	57	-1.8%
Calcium	mmol/l	2.29	2.39	2.43	4.4%	2.23	2.24	-2.6%
Cholesterol	mmol/l	4.18	4.59	4.61	9.8%	4.34	4.43	3.8%
Creatinkinase (CK)	U/l	193	185	187	-4.1%	181	194	-6.2%
Chloride	mmol/l	98	99	100	1.0%	98	98	0.0%
Creatinine	µmol/l	141	127	128	-9.9%	135	131	-4.3%
Direct Bilirubin	µmol/l	12.1	13.5	14.2	11.6%	11.6	12.6	-4.1%
gamma-GT	U/l	55	59	60	7.3%	60	61	9.1%
Glucose	mmol/l	6.27	6.69	6.89	6.7%	6.35	6.57	1.3%
Inorg. phosphorus	mmol/l	1.65	1.59	1.6	-3.6%	1.65	1.69	0.0%
Iron	µmol/l	19.2	22.8	23.2	18.8%	19.9	19.6	3.6%
Potassium	mmol/l	3.95	3.95	3.97	0.0%	4.1	4.1	3.8%
LDH	U/l	416	441	451	6.0%	415	417	-0.2%
Magnesium	mmol/l	0.92	0.97	0.97	5.4%	0.96	1.00	4.3%
Sodium	mmol/l	143	142	143	-0.7%	146	147	2.1%
Total Bilirubin	µmol/l	21.8	23	23.8	5.5%	20.2	21.6	-7.3%
Total Protein	g/l	59.5	57.9	61.2	-2.7%	58.1	59.1	-2.4%
Triglycerides	mmol/l	1.24	1.23	1.2	-0.8%	1.22	1.28	-1.6%

**Human**

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Urea	mmol/l	7.47	8.5	8.6	13.8%	7.50	7.59	0.4%
Uric Acid	mmol/l	0.35	0.354	0.357	1.1%	0.355	0.358	1.4%

SERODOS® Raw material LOT 178UE		Fresh	Check dates					
Parameter	Units	2002-01 Target	2004-02 4°C	-80°C	% DEV	4°C	-80°C	% DEV
Albumin	g/l	30	29.8	30	-0.7%	30.4	31.5	1.3
Alk. Phosphatase	U/l	515	490	515	-4.9%	489	477	-0.2
GPT (ALT)	U/l	124	124	124	0.0%	113	115	-8.9
GOT (AST)	U/l	157	154	157	-1.9%	144	145	-8.3
Calcium	U/l	3.27	3.23	3.27	-1.2%	3.03	3.11	-7.4
Chloride	mmol/l	118	117	118	-0.8%	117.7	119	-0.3
Creatinkinase (CK)	mmol/l	456	468	456	2.6%	434	451	-4.9
Creatinine	U/l	329	325	329	-1.2%	359	364	9.1
gamma-GT (GGT)	mmol/l	202	194	202	-4.0%	195	201	-3.5
Glucose	µmol/l	16.13	15.61	16.13	-3.2%	15.28	15.6	-5.3
Inorg. phosphorus	µmol/l	2.31	2.29	2.31	-0.9%	2.17	2.15	-6.1
LDH	U/l	677	672	677	-0.7%	668	685	-1.4
alpha-Amylase	mmol/l	333	357	363	-1.7%	326	333	-2.2
Magnesium	mmol/l	1.76	1.73	1.76	-1.7%	1.68	1.71	-1.8
Cholesterol	µmol/l	7.61	7.94	7.61	4.3%	7.56	7.65	-0.7
Triglycerides	mmol/l	2.7	2.69	2.7	-0.4%	2.6	2.71	-3.8
Iron	U/l	39.2	38.3	39.2	-2.3%	34.9	33.9	10.7
Total protein	mmol/l	46.1	45.1	46.1	-2.2%	43.5	44.1	-5.7
Bilirubin total	µmol/l	71.5	85.6	88.9	19.5%	70.6	71.5	-1.4
Bilirubin direct	µmol/l	27.1	28.5	29.6	5.1%	26.0	27.1	-4.1
Urea	g/l	20.23	19.66	20.23	-2.8%	19.18	19.3	-5.2
Sodium	mmol/l	166	164	166	-1.2%	162.1	165	-2.4
Uric Acid	mmol/l	0.57	0.55	0.57	-3.0%	0.59	0.58	3.5
Potassium	mmol/l	6.3	6.3	6.3	0.0%	6.21	6.2	-1.4%

SERODOS® Raw material LOT 141UE		Fresh	Check dates					
Parameter	Unit	2000-07 Target	2002-03			2005-02		
			4°C	-80°C	% DEV	4°C	-80°C	% DEV
Albumin	g/l	29.8	31.2	31	0.6	31.3	30.7	2.0%
Alk. Phosphatase	U/l	524	565	566	-0.2	534	530	0.8%
GPT (ALT)	U/l	131	141	143	-1.4	126	126	0.0%
Alpha-Amylase	U/l	376	345	344	0.3	393	392	0.3%
GOT (AST)	U/l	141	141	145	-2.8	132	134	-1.5%
Calcium	mmol/l	3.13	3.29	3.29	0.0	3.21	3.12	2.9%
Cholesterol	mmol/l	111	110	0.9	0.4	111	112	0.9%
CK-NAC	U/l	7.38	7.47	7.44	-2.9	7.65	7.77	-1.5%
Chloride	mmol/l	473	477	491	0.9	490	505	-3.0%
Creatinine	µmol/l	338	318	313	1.6	345	340	1.5%
Bilirubin direct	µmol/l	20.5	19.9	20.4	-2.5	19.0	18.7	1.6%
gamma-GT (GGT)	U/l	197	213	212	0.5	220	218	0.9%
Glucose	mmol/l	16.4	17.04	17.15	-0.6	16.97	17.04	-0.4%
Inorg. phosphorus	mmol/l	2.19	2.17	2.17	0.0	2.25	2.24	0.4%
Iron	µmol/l	37.5	39.3	39.9	-1.5	37.8	36.9	2.4%
Potassium	mmol/l	6.03	6.09	6.09	0.0	6.1	6.1	0.0%
LDH	U/l	711	731	731	0.0	721	722	-0.1%
Magnesium	mmol/l	1.75	1.69	1.69	0.0	1.82	1.79	1.7%
Sodium	mmol/l	158	158	158	0.0	161	159	1.3%
Bilirubin total	µmol/l	62.1	60.7	60.9	-0.3	59.7	58.5	2.1%
Total protein	g/l	43.3	42.3	41.4	2.2	42.2	41.8	1.0%
Triglycerides	mmol/l	2.63	2.68	2.69	-0.4	2.78	2.77	0.4%
Urea	mmol/l	19.5	19.35	19.8	-2.3	19.29	19.36	-0.4%

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Uric acid	mmol/l	0.57	0.584	0.585	-0.2	0.609	0.598	1.8%
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### Conclusion

The real-time stability data obtained observed from 3 independent LOT s over a period of 4 years confirm the stability claim of 4 years.

### 3.2 Stability after Reconstitution – SERODOS® plus

The stability after reconstitution has been checked at storage conditions 2...8 °C and 25 °C. The data are summarised below (units and parameters follow the above scheme).

#### Results

SERODOS® plus Raw material LOT 272UECM/2			Check dates					
Parameter	Unit	Target	Storage at 2...8 °C				Storage at 25 °C	
			4 days	% DEV	7 days	% DEV	8 hours	% DEV
Albumin	g/l	34.1	34.2	0.3%	34.4	0.9%	34	-0.3%
Alk. Phosphatase	U/l	342	355	3.8%	373	9.1%	361	5.6%
GPT (ALT)	U/l	150	147	-2.0%	144	-4.0%	144	-4.0%
alpha-Amylase	U/l	288	288	0.0%	295	2.4%	288	0.0%
GOT (AST)	U/l	154	150	-2.6%	149	-3.2%	153	-0.6%
Calcium	mmol/l	3.25	3.25	0.0%	3.26	0.3%	3.26	0.3%
Chloride	mmol/l	123.3	122.5	-0.6%	124.3	0.8%	123.2	-0.1%
Cholesterol	mmol/l	6.29	6.38	1.4%	6.3	0.2%	6.29	0.0%
Creatinkinase (CK)	U/l	443.3	444.8	0.3%	436	-1.6%	439.1	-0.9%
Creatinine	µmol/l	429.8	431.1	0.3%	429.8	0.0%	432.3	0.6%
Bilirubin direct	g/l	20.7	19.9	-3.9%	19.8	-4.3%	20	-3.4%
gamma-GT (GGT)	U/l	159.6	159.5	-0.1%	160.3	0.4%	158.9	-0.4%
Glucose	mmol/l	13.91	14.15	1.7%	14.1	1.4%	13.81	-0.7%
Iron	µmol/l	34.4	35.3	2.6%	36	4.7%	35.5	3.2%
LDH	U/l	1102	1103	0.1%	1101	-0.1%	1103	0.1%
Lithium	mmol/l	2.109	2.066	-2.0%	2.104	-0.2%	2.111	0.1%
Magnesium	mmol/l	1.51	1.55	2.6%	1.58	4.6%	1.48	-2.0%
Inorg. phosphorus	mmol/l	2.97	2.98	0.3%	2.94	-1.0%	2.89	-2.7%
Potassium	mmol/l	7.19	7.04	-2.1%	7.24	0.7%	7.11	-1.1%
Sodium	mmol/l	163.2	162.1	-0.7%	164.3	0.7%	162.8	-0.2%
Bilirubin total	g/l	90.7	86	-5.2%	85.2	-6.1%	87.3	-3.7%
Total protein	g/l	51	50.5	-1.0%	51.3	0.6%	50.7	-0.6%
Triglycerides	mmol/l	2.792	2.912	4.3%	2.911	4.3%	2.83	1.4%
Urea	mmol/l	25.03	24.96	-0.3%	25.18	0.6%	25.57	2.2%
Uric acid	mmol/l	0.628	0.622	-1.0%	0.636	1.3%	0.622	-1.0%

### Conclusion

The stability data after reconstitution confirm a stability of at least 8 hours at 25°C and at least 7 days at 2..8°C for the parameters listed above.

### LOT-specific Deviations

SERODOS® plus LOT 0007			Check dates				
			Storage at 2...8°C				
Parameter	Unit	Target	Fresh	8 days	% DEV	11 days	% DEV
HDL Cholesterol	mg/dl	140	137	126	-5.9%	130	-5.0
LDL Cholesterol	mg/dl	129	137	132	-3.5%	138	1.0

#### Conclusion

The stability data after reconstitution confirm the claimed stability at 2..8 °C for at least 7 days.

SERODOS® plus LOT 0007			Check dates				
			Storage at 2...8°C				
Parameter	Unit	Target	Fresh	5 days	% DEV	8 days	% DEV
Glucose	mg/dl	198	195	195	0	-	-

#### Conclusion

The stability data after reconstitution confirm stability at 2..8°C for at least 4 days.

SERODOS® plus LOT 0008			Check dates						
			Storage at 2...8°C						
Parameter	Unit	Target	Fresh	1 day	% DEV	2 days	% DEV	8 days	% DEV
Bilirubin direct	mg/dl	2.96	3.07	2.90	-5.4	2.76	-10	-	-
Bilirubin total	mg/dl	4.67	4.87	4.57	-6.1	4.34	-11	-	-

#### Conclusion

The stability data after reconstitution confirm stability at 2..8°C for Bilirubin direct/Bilirubin total for 2 days.

### 3.3 Stability after Reconstitution – SERODOS®

#### 3.3.1 Analyte stability

The stability of the analytes in SERODOS® control sera was tested with HUMAN multipurpose or system reagents. The measurements were carried out on HumaStar analysers and Humalyzers.

After reconstitution (= day 0/fresh) the SERODOS® control material was stored up to 7 days at 2 – 8°C. For the determination of acid phosphatase, the control material was not stabilized after reconstitution.

The mean values (n = 4) from fresh and stored control material were calculated and compared. The acceptance criterion for the deviation between freshly reconstituted and stored control serum was set at '≤10 %Dev'.

SERODOS® raw material LOT 210405A, final product LOT 0006						
Analyte name	Unit	Analyser	Storage at 2 – 8 °C			
			Day 0 / Mean	No. of Days	Mean	%Dev
Acid phosphatase	U/l	HumaStar 600	1.91	7	1.82	-4.7
Albumin	g/dl	HumaStar 600	2.96	7	2.97	0.4
alpha-Amylase	U/l	HumaStar 600	91.3	7	92.5	1.3
Alk. Phosphatase (DGKC)	U/l	HumaStar 600	163	7	167	2.0
Alk. Phosphatase (IFCC)	U/l	HumaStar 600	106	7	111	4.7
Apolipoprotein A1	mg/dl	HumaStar 600	61.3	7	55.2	-9.9
Apolipoprotein B	mg/dl	HumaStar 600	44.3	7	42.3	-4.6
Bilirubin direct	mg/dl	HumaStar 600	0.83	1	0.76	-8.4
Bilirubin total	mg/dl	HumaStar 600	1.05	1	0.98	-6.3
Calcium	mg/dl	HumaStar 600	8.62	7	8.19	-5.1
Cholinesterase	U/l	HumaStar 600	3802	7	3884	2.2
Chloride	mmol/l	HumaStar 600	95.5	7	96.3	0.8
Cholesterol	mg/dl	HumaStar 600	163	7	175	7.1

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CK	U/l	HumaStar 600	128	5	118	-8.0
Creatinine (Jaffé)	mg/dl	HumaStar 600	1.15	7	1.17	1.7
Creatinine (enzyme)	mg/dl	HumaStar 600	0.92	7	0.87	-5.4
gamma-GT	U/l	HumaStar 600	34.3	7	35.3	2.8
GOT (ASAT) IFCC	U/l	HumaStar 600	32.5	2	33.7	3.8
GPT (ALAT) IFCC	U/l	HumaStar 600	35.5	2	38.8	9.5
Glucose	mg/dl	HumaStar 600	91.4	2	84.1	-8.0
Immunoglobulin IgA	mg/dl	HumaStar 600	158	7	161	2.1
Immunoglobulin IgA	mg/dl	HumaStar 100	152	7	172	13.2
Immunoglobulin IgG	mg/dl	HumaStar 600	683	7	697	2.1
Immunoglobulin IgM	mg/dl	HumaStar 600	48.6	7	50.2	3.3
Immunoglobulin IgM	mg/dl	HumaStar 100	53.4	7	82.3	54.1
Iron (CAB)	µg/dl	HumaStar 200	127	7	125	-1.1
Iron (TPTZ)	µg/dl	HumaStar 600	94.7	7	89.9	-5.1
Iron (TPTZ)	µg/dl	HumaStar 100	75.5	7	51.0	-32.5
LDH SCE	U/l	HumaStar 600	396	7	387	-2.4
Lipase	U/l	HumaStar 600	34.0	7	35.2	3.6
Lipoprotein (a)	mg/dl	HumaStar 600	37.4	7	39.6	5.8
Magnesium	mg/dl	HumaStar 600	2.27	7	2.21	-2.7
Inorg. phosphorus	mg/dl	HumaStar 600	3.46	7	3.16	-8.5
Potassium	mmol/l	HumaStar 600	4.56	7	5.06	11.0
Sodium	mmol/l	HumaStar 600	107	7	109	2.4
Total protein	g/dl	HumaStar 600	5.30	7	5.27	-0.7
TIBC (CAB)	µg/dl	HumaStar 200	286	7	296	3.6
Triglycerides	mg/dl	HumaStar 600	143	7	138	-3.6
Urea	mg/dl	HumaStar 600	30.8	7	31.9	3.4
Uric acid	mg/dl	HumaStar 600	4.45	7	4.24	-4.7
<b>SERODOS® raw material LOT 210405A, final product LOT 0006</b>						
Creatinine (Jaffé)	mg/dl	HumaLyzor 4000	0.95	7	0.76	-24.0

The acceptance criterion for stability after reconstitution was not met for

- Potassium on HumaStar 600,
- Immunoglobulins IgA and IgM, Iron (TPTZ) on HumaStar 100
- Creatinine (Jaffé) on HumaLyzor 4000, when the auto-Creatinine liquicolor kit is used

### Conclusion

All analytes except acid phosphatase: The stability data after reconstitution confirm the claimed stability at 2...8 °C for at least 7 days.

### LOT- specific Deviations

SERODOS® LOT 0008			Check dates						
			Storage at 2...8 °C						
Parameter	Unit	Target	Fresh	1 day	% DEV	2 days	% DEV	8 days	% DEV
Bilirubin direct	mg/dl	0.73	0.71	0.67	-4.8	0.64	-9.6	0.58	-18.4
Bilirubin total	mg/dl	1.02	0.97	0.92	-5.3	0.88	-9.3	0.77	-20.4
Glucose	mg/dl	88.2	86.0	81.4	-5.3	67.9	-21.0	53.4	-37.8
GOT (AST)	U/l	30.8	30.6	30.9	0.98	31.4	2.6	47.0	53.6
Parameter	Unit	Target	Fresh	1 day	% DEV	5 days	% DEV	8 days	% DEV
GPT (ALT)	U/l	36.0	33.7	34.3	2.0	35.0	4.1	38.3	13.8

### Conclusion

The stability data after reconstitution confirm stability at 2..8 °C for Bilirubin direct/Bilirubin total and GOT (AST) for 2 days, for GPT (ALT) for 5 days and for Glucose 1 day.

### 3.3.1 Intrinsic turbidity

The intrinsic turbidity of the SERODOS® control material was determined by measuring the optical density (OD) at 710 nm on a Shimadzu photometer. 3 control vials were reconstituted according to the manufacturer's instruction and stored at 2-8 °C for 7 days. The mean value (n=3) was calculated and compared with the max. allowable OD value ≤0.65.

SERODOS® LOT 0006, OD results obtained on a Shimadzu photometer								
Vial No.	Fresh (Day 0)	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Control vial 1	0.359	0.505	0.670	0.606	0.479	0.731	0.568	1.085
Control vial 1	0.266	0.587	0.598	0.387	0.532	0.688	0.695	1.043
Control vial 1	0.335	0.614	0.464	0.495	0.454	0.762	0.688	0.879
<b>Mean</b>	<b>0.320</b>	<b>0.569</b>	<b>0.577</b>	<b>0.496</b>	<b>0.488</b>	<b>0.727</b>	<b>0.650</b>	<b>1.002</b>

On the 5<sup>th</sup> day after reconstitution, the allowable OD value was exceeded. Considering the different analyzer settings with/without blank correction and the intrinsic turbidity of the control material, the following stabilities after reconstitution and storage at 2 – 8 °C were determined for the analytes in SERODOS® control sera:

Analyte	Stability at 2-8 °C
Acid phosphatase, Albumin, alpha-Amylase, Alkaline phosphatase, Apolipoprotein A1/B, Calcium, Chloride, Cholesterol, Creatinine <sup>1</sup> , Immunoglobulin IgG, LDH, Lipase, Lipoprotein (a), Magnesium, Sodium, TIBC (CAB), Total protein, Triglycerides, Urea, Uric acid <sup>1</sup> HumaStar analysers	7 days
CK, Phosphorus inorganic, Potassium	4 days
Glucose	2 days
Bilirubin direct, Bilirubin total, Creatinine <sup>2</sup> , GOT (ASAT), GPT (ALAT), Immunoglobulins IgA, IgM, Iron, TIBC <sup>2</sup> auto-CREATININE liquicolor on HumaLyzer 4000	1 day

### Conclusion

The proven analyte stability after reconstitution and storage at 2-8°C confirm the suitability of SERODOS® control sera for use in routine laboratories.

### 3.4 Stability after Reconstitution and Storage at –20°C for one month

The data are summarised below (units and parameters follow the above scheme).

SERODOS® plus - Raw material LOT 281UE/1		Storage at -20°C		
Parameter	Unit	Target	1 month	%DEV
Albumin	g/l	26.5	26.9	1.5%
Alkaline Phosphatase	U/l	522	504	-3.4%
GPT (ALT)	U/l	138	134	-2.9%
alpha-Amylase	U/l	314	312	-0.6%
GOT (AST)	U/l	155	152	-1.9%
Calcium	mmol/l	3.51	3.48	-0.9%
Chloride	mmol/l	111.8	111.9	0.1%
Cholesterol	mmol/l	7.45	7.42	-0.4%
Creatinkinase (CK)	U/l	563.2	536.8	-4.7%
Creatinine	µmol/l	353	363.1	2.9%
Bilirubin direct	µmol/l	32.7	23.3	-28.7%
gamma-GT (GGT)	U/l	192.1	191.7	-0.2%
Glucose	mmol/l	15.78	15.4	-2.4%
Iron	µmol/l	36.7	35.6	-3.0%
LDH	U/l	813	801	-1.5%
Lithium	mmol/l	2.181	2.125	-2.6%

Magnesium	mmol/l	1.87	1.88	0.5%
Inorg. phosphorus	mmol/l	2.26	2.25	-0.4%
Potassium	mmol/l	6.03	6.14	1.8%
Sodium	mmol/l	157.4	159.2	1.1%
Bilirubin total	µmol/l	90.9	68.1	-25.1%
Total protein	g/l	41.6	41.7	0.2%
Triglycerides	mmol/l	2.849	2.848	0.0%
Urea	mmol/l	19.58	19.56	-0.1%
Uric acid	mmol/l	0.59	0.591	0.2%

#### Conclusion

The claimed stability after reconstitution and storage at -20°C for one month is confirmed.

#### 4 Result Documentation

For each LOT of SERODOS® control sera a leaflet is created which contains information on reconstitution, handling, stability, target values and permitted ranges for all specified parameters.

#### 5 Traceability

The assigned control values of the SERODOS® control sera are traceable to reference materials or methods, which are indicated on the respective calibration values sheets or instruction for use of the calibration material.