510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K211485

B Applicant

Diagnostica Stago SAS

C Proprietary and Established Names

STA - NeoPTimal

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
GJS	Class II	21 CFR 864.7750 - Prothrombin Time Test	HE - Hematology

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Prothrombin Time (PT) in seconds and International Normalized Ratio (INR)

C Type of Test:

Quantitative

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The STA - NeoPTimal kits provide thromboplastin reagents from rabbit brain extract, for the quantitative determination, in human citrated plasma (3.2% sodium citrate), of Prothrombin Time (PT) on STA-R family, STA Compact family and STA Satellite family instruments. STA - NeoPTimal is a coagulation screening test intended to be used by professional laboratory personnel for the evaluation of the extrinsic coagulation pathway and the monitoring of oral vitamin K antagonist therapy using the International Normalized Ratio (INR).

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

STA-R family includes STA-R (K983460), STA-R Evolution (K093001) and STA R Max (K151867).
STA Compact family contains STA Compact (K093167) and STA Compact Max (K130090).
STA Satellite family contains STA Satellite (K082248).

IV Device/System Characteristics:

A Device Description:

The in vitro diagnostic STA - NeoPTimal kits are available in two sizes and contain:

STA - NeoPTimal 5	STA - NeoPTimal 10
6 x 5 ml vials of Reagent 1	12 x 10 ml vials of Reagent 1
6 x 5 ml vials of Reagent 2	12 x 10 ml vials of Reagent 2

Reagent 1 in STA - NeoPTimal is lyophilized thromboplastin prepared from rabbit brain extract. The STA - NeoPTimal reagent contains a specific heparin inhibitor. Reagent 2 is a solvent containing calcium.

B Principle of Operation:

The STA - NeoPTimal, an in vitro diagnostic test consists of the use of calcium thromboplastin to measure the clotting time (formation of a fibrin clot) of the patient's plasma and to compare it with that of a normal standard (MNPT). The test measures, as a whole, the activities of the coagulation factor II (prothrombin), factor V (proaccelerin), factor VII (proconvertin), factor X (Stuart factor) and factor I (fibrinogen).

V Substantial Equivalence Information:

A Predicate Device Name(s):

Thromborel S

B Predicate 510(k) Number(s):

K003870

C Comparison with Predicate(s):

Device & Predicate Device(s):	K211485	K003870
Device Trade Name	STA - NeoPTimal	Thromborel S
General Device Characteristic Similarities		
Intended Use/Indications For Use	The STA®- NeoPTimal kits provide thromboplastin reagents from rabbit brain extract, for the quantitative determination, in human citrated plasma (3.2% sodium citrate), of Prothrombin Time (PT) on STA-R®family, STA Compact® family and STA Satellite® family instruments. STA®-NeoPTimal is a coagulation screening test intended to be used by professional laboratory personnel for the evaluation of the extrinsic coagulation pathway and the monitoring of oral vitamin K antagonist therapy using the International Normalized Ratio (INR).	Thromborel S Reagent is used for the determination of the Prothrombin Time (PT) according to Quick and, in conjunction with the relevant deficient plasmas, for the determination of the coagulation factor II, V, VII and X.
Assay Method	Clotting Time	Same
Test Principle	The STA - NeoPTimal test consists of the use of calcium thromboplastin to measure the clotting time of the patient's plasma and	The Thromborel S test is a coagulation process triggered by incubation of plasma with thromboplastin and calcium. The time to formation of a fibrin

	to compare it with that of a normal standard. The test measures, as a whole, the activity of the coagulation factor II (prothrombin), factor V (proaccelerin), factor VII (proconvertin), factor X (Stuart factor) and factor I (fibrinogen).	clot is then measured.
General Device Characteristic Differences		
Thromboplastin source	Rabbit brain	Human placenta
Analyzers	STA-R Family, STA Compact Family and STA Satellite Family	Sysmex CA series and Siemens BCS series

VI Standards/Guidance Documents Referenced:

- CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition
- CLSI H47-A2: One-Stage Prothrombin Time (PT) Test and Activated Partial Thromboplastin Time (aPTT) Test; Approved Guideline – Second Edition
- CLSI H48: Determination of Coagulation Factor Activities Using the One-Stage Clotting Assay; 2nd Edition
- CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition
- CLSI EP07: Interference Testing in Clinical Chemistry; 3rd Edition
- CLSI EP25-A: Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline
- CLSI EP28-A3c: Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition
- CLSI H21-A5: Collection, Transport, and Processing of Blood Specimens for Testing Plasma- Based Coagulation Assays and Molecular Hemostasis Assays; Approved Guideline – Fifth Edition
- CLSI H54-A: Procedures for Validation of INR and Local Calibration of PT-INR Systems; Approved Guideline – First Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. <u>Precision/Reproducibility:</u>

Repeatability was assessed with three lots of STA - NeoPTimal on a representative of each analyzer family: STA-R, STA Compact and STA Satellite. The study was conducted using four lots of reagents at one external site. The study was conducted for 20 days with two runs per day and two replicates per run by two operators. The STA - NeoPTimal test demonstrated acceptable repeatability when evaluated using control materials and 3.2% citrated plasma patient samples. The repeatability results for a representative of each analyzer family for PT in seconds and INR are summarized below.

Repeatability on STA-R, PT in seconds

All Lots (seconds)			Repeatability		Between-run		Between-day		Between-lot		Within-lab	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal 1	240	14.270	0.119	0.83	0.140	0.98	0.201	0.57	0.000	0.00	0.201	1.41
Normal 2	240	13.861	0.126	0.91	0.132	0.95	0.210	0.75	0.000	0.00	0.210	1.52
VKA 2≤INR≤3	240	30.888	0.341	1.10	0.700	2.27	0.838	1.00	0.248	0.80	0.838	2.71
VKA 3<INR≤4	240	45.502	0.416	0.91	0.951	2.09	1.038	0.00	0.364	0.80	1.038	2.28
VKA 4.5<INR≤5.5	240	62.892	0.527	0.84	1.413	2.25	1.594	0.82	0.471	0.75	1.594	2.53
VKA> 5.5	240	70.665	0.783	1.11	2.062	2.92	2.206	0.00	0.456	0.65	2.206	3.12
Def V	240	26.270	0.339	1.29	0.520	1.98	0.621	0.00	0.190	0.72	0.621	2.36
*SCN	240	14.831	0.138	0.93	0.138	0.93	0.202	0.35	0.028	0.19	0.202	1.36
*SCP	240	26.111	0.256	0.98	0.656	2.51	0.712	0.41	0.000	0.00	0.712	2.73
^CCN+	240	14.908	0.125	0.84	0.184	1.23	0.222	0.00	0.000	0.00	0.222	1.49
^CCABN+	240	38.953	0.307	0.79	1.056	2.71	1.100	0.00	0.000	0.00	1.100	2.82

*SCN: STA – System Control N, SCP: STA– System Control P, Normal and Abnormal Control Materials
^CCN+ : STA – Coag Control N Plus, CCABN+ : Coag Control ABN Plus, Normal and Abnormal Control Materials

Repeatability on STA-R, INR

All Lots (INR)			Repeatability		Between-run		Between-day		Between-lot		Within-lab	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal 1	240	1.042	0.010	0.96	0.010	0.96	0.015	0.58	0.014	1.34	0.015	1.47
Normal 2	240	1.012	0.009	0.89	0.010	0.99	0.015	0.69	0.015	1.48	0.015	1.50
VKA 2≤INR≤3	240	2.317	0.027	1.17	0.054	2.33	0.065	0.99	0.050	2.16	0.065	2.79
VKA 3<INR≤	240	3.458	0.032	0.93	0.075	2.17	0.082	0.00	0.095	2.75	0.082	2.36
VKA 4.5<INR≤5.5	240	4.832	0.042	0.87	0.114	2.36	0.128	0.83	0.151	3.13	0.128	2.65
VKA> 5.5	240	5.451	0.062	1.14	0.164	3.01	0.175	0.00	0.170	3.12	0.175	3.22
^CCN+	240	1.091	0.010	0.92	0.014	1.28	0.017	0.00	0.016	1.47	0.017	1.58

^CCN+ : STA – Coag Control N Plus, CCABN+ : Coag Control ABN Plus, Normal and Abnormal Control Materials

Repeatability on STA Compact Max, PT in seconds

All Lots (seconds)			Repeatability		Between-run		Between-day		Between-lot		Within-lab	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal 1	240	14.401	0.191	1.33	0.159	1.10	0.260	0.52	0.000	0.00	0.260	1.80
Normal 2	240	14.132	0.209	1.48	0.246	1.74	0.353	1.00	0.000	0.00	0.353	2.50
VKA 2≤INR≤3	240	29.531	0.589	1.99	1.053	3.57	1.207	0.00	0.136	0.46	1.207	4.09
VKA	240	44.070	0.870	1.97	1.635	3.71	1.852	0.00	0.478	1.08	1.852	4.20

All Lots (seconds)			Repeatability		Between-run		Between-day		Between-lot		Within-lab	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
3<INR≤4												
VKA 4.5<INR≤5.5	240	61.342	0.974	1.59	2.791	4.55	2.956	0.00	0.474	0.77	2.956	4.82
VKA>5.5	240	69.433	1.444	2.08	3.209	4.62	3.519	0.00	0.289	0.42	3.519	5.07
Def V	240	25.510	0.420	1.65	0.924	3.62	1.015	0.00	0.177	0.69	1.015	3.98
*SCN	240	14.865	0.236	1.59	0.203	1.37	0.324	0.61	0.000	0.00	0.324	2.18
*SCP	240	25.030	0.402	1.61	0.890	3.56	0.977	0.00	0.196	0.78	0.977	3.90
^CCN+	240	14.929	0.263	1.76	0.139	0.93	0.332	0.99	0.000	0.00	0.332	2.23
^CCABN+	240	37.850	0.625	1.65	1.188	3.14	1.342	0.00	0.408	1.08	1.342	3.55

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^CCN+ : STA – Coag Control N Plus, CCABN+ : Coag Control ABN Plus, Normal and Abnormal Control Materials

Repeatability on STA Compact Max, INR

All Lots (INR)			Repeatability		Between-run		Between-day		Between-lot		Within-lab	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal 1	240	1.053	0.014	1.33	0.012	1.14	0.006	0.57	0.018	1.71	0.019	1.84
Normal 2	240	1.032	0.016	1.55	0.019	1.84	0.010	0.97	0.016	1.55	0.027	2.59
VKA 2≤INR≤3	240	2.213	0.046	2.08	0.082	3.71	0.000	0.00	0.067	3.03	0.094	4.25
VKA 3<INR≤4	240	3.348	0.067	2.00	0.129	3.85	0.000	0.00	0.144	4.30	0.145	4.34
VKA 4.5<INR≤5.5	240	4.711	0.078	1.66	0.222	4.71	0.000	0.00	0.204	4.33	0.235	4.99
VKA>5.5	240	5.355	0.115	2.15	0.257	4.80	0.000	0.00	0.237	4.43	0.282	5.26
^CCN+	240	1.093	0.020	1.83	0.011	1.01	0.011	1.01	0.019	1.74	0.025	2.32

^CCN+ : STA – Coag Control N Plus, CCABN+ : Coag Control ABN Plus, Normal and Abnormal Control Materials

Repeatability on STA Satellite, PT in seconds

All Lots (seconds)			Repeatability		Between-run		Between-day		Between-lot		Within-lab	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal 1	240	14.108	0.139	0.99	0.218	1.55	0.000	0.00	0.112	0.79	0.259	1.83
Normal 2	240	13.639	0.165	1.21	0.202	1.48	0.000	0.00	0.136	1.00	0.261	1.91
VKA 2≤INR≤3	240	29.791	0.439	1.47	0.731	2.45	0.000	0.00	0.000	0.00	0.853	2.86
VKA 3<INR≤4	240	44.366	0.695	1.57	0.983	2.22	0.313	0.71	0.563	1.27	1.244	2.80
VKA INR> 4.5	240	64.173	0.688	1.07	2.063	3.21	0.227	0.35	0.666	1.04	2.187	3.41
VKA INR>4.5	240	71.376	1.334	1.87	2.307	3.23	0.000	0.00	0.590	0.83	2.665	3.73
Def V	240	24.988	0.267	1.07	0.505	2.02	0.000	0.00	0.000	0.00	0.571	2.29
*SCN	240	14.557	0.221	1.52	0.242	1.66	0.081	0.56	0.025	0.17	0.338	2.32
*SCP	240	25.170	0.345	1.37	0.709	2.82	0.000	0.00	0.000	0.00	0.788	3.13
^CCN+	240	14.665	0.140	0.95	0.172	1.17	0.070	0.48	0.074	0.50	0.233	1.59
^CCABN+	240	38.025	0.559	1.47	1.211	3.18	0.000	0.00	0.266	0.70	1.334	3.51

*SCN: STA – System Control N, SCP: STA– System Control P, Normal and Abnormal Control Materials
^CCN+ : STA – Coag Control N Plus, CCABN+ : Coag Control ABN Plus, Normal and Abnormal Control Materials

Repeatability on STA Satellite, INR

All Lots (INR)			Repeatability		Between-run		Between-day		Between-lot		Within-lab	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal 1	240	1.038	0.011	1.06	0.016	1.54	0.000	0.00	0.009	0.87	0.019	1.87
Normal 2	240	1.003	0.013	1.30	0.016	1.59	0.000	0.00	0.009	0.90	0.021	2.05
VKA 2≤INR≤3	240	2.255	0.034	1.51	0.057	2.53	0.000	0.00	0.042	1.86	0.066	2.94
VKA 3<INR≤4	240	3.408	0.055	1.61	0.080	2.35	0.026	0.76	0.103	3.02	0.101	2.95
VKA INR>4.5	240	4.997	0.055	1.10	0.166	3.32	0.014	0.28	0.163	3.26	0.175	3.51
VKA INR>4.5	240	5.580	0.108	1.94	0.190	3.41	0.000	0.00	0.181	3.24	0.219	3.92
^CCN+	240	1.081	0.012	1.11	0.013	1.20	0.006	0.55	0.013	1.20	0.019	1.73

*SCN: STA – System Control N, SCP: STA– System Control P, Normal and Abnormal Control Materials
^CCN+ : STA – Coag Control N Plus, CCABN+ : Coag Control ABN Plus, Normal and Abnormal Control Materials

A multi-site reproducibility study was performed at three clinical sites. The study was assessed using three lots of STA - NeoPTimal on a representative of each analyzer family: STA-R, STA Compact and STA Satellite. The study conducted for five days with two runs per day and three replicates per run by a minimum of two operators. The STA - NeoPTimal demonstrated acceptable reproducibility when evaluated using control material and 3.2% citrated patient plasma samples. The reproducibility study results for a representative of each analyzer family for PT in seconds and INR are summarized in tables below.

Summary of Multi-Site Reproducibility Results on STA-R Max in PT seconds

All Data (seconds)			Repeatability		Between-run		Between-day		Between-lot		Between-site		Reproducibility	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal 1	270	14.662	0.139	0.95	0.153	1.04	0.000	0.00	0.016	0.11	0.396	2.70	0.447	3.05
Normal 2	270	14.272	0.137	0.96	0.142	0.99	0.000	0.00	0.005	0.04	0.420	2.94	0.464	3.25
VKA 2≤INR≤3	270	31.279	0.298	0.95	0.584	1.87	0.000	0.00	0.242	0.77	0.837	2.68	1.090	3.48
VKA 3<INR≤4	270	46.034	0.358	0.78	0.905	1.97	0.000	0.00	0.359	0.78	0.999	2.17	1.440	3.13
VKA 4.5<INR≤5.5	270	63.011	0.505	0.80	1.251	1.99	0.000	0.00	0.753	1.20	1.288	2.04	2.011	3.19
VKA >5.5	270	71.215	0.727	1.02	1.393	1.96	0.000	0.00	0.796	1.12	1.895	2.66	2.587	3.63
Def V	270	26.671	0.241	0.90	0.508	1.90	0.000	0.00	0.244	0.91	0.605	2.27	0.861	3.23
*SCN	270	15.267	0.159	1.04	0.192	1.26	0.000	0.00	0.000	0.00	0.358	2.34	0.436	2.86
*SCP	270	26.298	0.235	0.89	0.503	1.91	0.000	0.00	0.181	0.69	0.435	1.65	0.728	2.77
^CCN+	270	15.269	0.174	1.14	0.138	0.90	0.000	0.00	0.040	0.26	0.384	2.51	0.446	2.92
^CCABN+	270	39.033	0.335	0.86	1.007	2.58	0.000	0.00	0.219	0.56	0.672	1.72	1.275	3.27

*SCN: STA – System Control N, SCP: STA– System Control P, Normal and Abnormal Control Materials
^CCN+ : STA – Coag Control N Plus, CCABN+ : Coag Control ABN Plus, Normal and Abnormal Control Materials

Summary of Multi-Site Reproducibility Results on STA-R Max, INR

All Data (INR)			Repeatability		Between-run		Between-day		Between-lot		Between-site		Reproducibility	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal 1	270	1.072	0.010	0.93	0.012	1.12	0.000	0.00	0.016	1.49	0.029	2.70	0.036	3.36
Normal 2	270	1.043	0.010	0.96	0.012	1.15	0.000	0.00	0.016	1.53	0.030	2.88	0.037	3.55
VKA 2≤INR≤3	270	2.347	0.023	0.98	0.046	1.96	0.000	0.00	0.048	2.04	0.059	2.51	0.092	3.92

All Data (INR)			Repeatability		Between-run		Between-day		Between-lot		Between-site		Reproducibility	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
VKA 3<INR≤4	270	3.500	0.028	0.80	0.072	2.06	0.000	0.00	0.086	2.46	0.063	1.80	0.132	3.77
VKA INR>4.5	270	4.840	0.041	0.85	0.100	2.07	0.000	0.00	0.116	2.40	0.084	1.74	0.180	3.72
VKA INR>4.5	270	5.494	0.057	1.04	0.112	2.04	0.000	0.00	0.149	2.71	0.129	2.35	0.234	4.26
^CCN+	270	1.119	0.013	1.16	0.011	0.98	0.000	0.00	0.015	1.34	0.028	2.50	0.036	3.22

*SCN: STA – System Control N, SCP: STA– System Control P, Normal and Abnormal Control Materials
^CCN+ : STA – Coag Control N Plus, CCABN+ : Coag Control ABN Plus, Normal and Abnormal Control Materials

Summary of Multi-Site Reproducibility Results on STA Compact Max in PT seconds

All Data (seconds)			Repeatability		Between-run		Between-day		Between-lot		Between-site		Reproducibility	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal 1	270	14.622	0.182	1.24	0.186	1.27	0.094	0.64	0.126	0.86	0.276	1.89	0.411	2.81
Normal 2	270	14.291	0.182	1.27	0.242	1.69	0.000	0.00	0.138	0.97	0.171	1.20	0.374	2.62
VKA 2≤INR≤3	270	30.786	0.604	1.96	0.645	2.10	0.107	0.35	0.294	0.95	1.283	4.17	1.589	5.16
VKA 3<INR≤4	270	45.475	0.627	1.38	1.098	2.41	0.414	0.91	0.292	0.64	1.241	2.73	1.843	4.05
VKA 4.5<INR≤5.5	270	62.711	0.917	1.46	1.773	2.83	0.582	0.93	0.000	0.00	1.665	2.66	2.664	4.25
VKA >5.5	270	70.780	1.379	1.95	2.379	3.36	0.000	0.00	0.621	0.88	2.317	3.27	3.649	5.16
Def V	270	26.370	0.411	1.56	0.563	2.14	0.000	0.00	0.500	1.90	0.850	3.22	1.207	4.58
*SCN	270	15.233	0.182	1.19	0.237	1.56	0.000	0.00	0.113	0.74	0.323	2.12	0.454	2.98
*SCP	270	26.111	0.436	1.67	0.558	2.14	0.000	0.00	0.229	0.88	0.902	3.45	1.170	4.48
^CCN+	270	15.190	0.174	1.15	0.266	1.75	0.000	0.00	0.103	0.68	0.248	1.63	0.416	2.74
^CCABN+	270	39.131	0.544	1.39	0.926	2.37	0.000	0.00	0.381	0.97	1.199	3.06	1.654	4.23

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^CCN+ : STA – Coag Control N Plus, CCABN+ : Coag Control ABN Plus, Normal and Abnormal Control Materials

Summary of Multi-Site Reproducibility Results on STA Compact Max, INR

All Data (INR)			Repeatability		Between-run		Between-day		Between-lot		Between-site		Reproducibility	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal 1	270	1.070	0.014	1.31	0.014	1.31	0.008	0.75	0.026	2.43	0.016	1.50	0.038	3.55
Normal 2	270	1.044	0.014	1.34	0.018	1.72	0.000	0.00	0.027	2.59	0.000	0.00	0.035	3.35
VKA 2≤INR≤3	270	2.310	0.046	1.99	0.050	2.16	0.007	0.30	0.085	3.68	0.088	3.81	0.140	6.06
VKA 3<INR≤4	270	3.457	0.050	1.45	0.087	2.52	0.030	0.87	0.139	4.02	0.057	1.65	0.183	5.29
VKA 4.5<INR≤5.5	270	4.819	0.073	1.51	0.143	2.97	0.043	0.89	0.189	3.92	0.074	1.54	0.262	5.44
VKA >5.5	270	5.462	0.111	2.03	0.193	3.53	0.000	0.00	0.236	4.32	0.131	2.40	0.350	6.41
^CCN+	270	1.113	0.014	1.26	0.021	1.89	0.000	0.00	0.026	2.34	0.013	1.17	0.038	3.42

Summary of Multi-Site Reproducibility Results on STA Satellite in PT seconds

All Data (seconds)			Repeatability		Between-run		Between-day		Between-lot		Between-site		Reproducibility	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal 1	270	14.370	0.166	1.16	0.203	1.41	0.000	0.00	0.196	1.36	0.225	1.57	0.397	2.76
Normal 2	270	13.957	0.130	0.93	0.216	1.55	0.000	0.00	0.200	1.43	0.223	1.60	0.392	2.81

All Data (seconds)			Repeatability		Between-run		Between-day		Between-lot		Between-site		Reproducibility	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
VKA 2≤INR≤3	270	31.016	0.510	1.64	1.039	3.35	0.000	0.00	0.534	1.72	1.251	4.03	1.786	5.76
VKA 3<INR≤4	270	46.346	0.600	1.29	1.110	2.40	0.000	0.00	0.744	1.61	1.484	3.20	2.085	4.50
VKA INR>4.5	270	66.456	0.829	1.25	1.457	2.19	0.212	0.32	0.836	1.26	1.893	2.85	2.672	4.02
VKA INR>4.5	270	74.733	1.331	1.78	2.262	3.03	0.000	0.00	1.455	1.95	3.260	4.36	4.432	5.93
Def V	270	25.763	0.387	1.50	0.532	2.06	0.000	0.00	0.180	0.70	0.776	3.01	1.033	4.01
*SCN	270	14.878	0.220	1.48	0.241	1.62	0.000	0.00	0.229	1.54	0.385	2.59	0.554	3.72
*SCP	270	25.845	0.372	1.44	0.573	2.22	0.000	0.00	0.375	1.45	0.741	2.87	1.075	4.16
^CCN+	270	14.926	0.154	1.03	0.229	1.53	0.000	0.00	0.180	1.21	0.309	2.07	0.452	3.03
^CCABN+	270	39.160	0.618	1.58	1.013	2.59	0.000	0.00	0.848	2.17	1.130	2.89	1.845	4.71

*SCN: STA – System Control N, SCP: STA– System Control P, Normal and Abnormal Control Materials
^CCN+ : STA – Coag Control N Plus, CCABN+ : Coag Control ABN Plus, Normal and Abnormal Control Materials

Summary of Multi-Site Reproducibility Results on STA Satellite, INR

All Data (seconds)			Repeatability		Between-run		Between-day		Between-lot		Between-site		Reproducibility	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal 1	270	1.059	0.012	1.13	0.016	1.51	0.000	0.00	0.020	1.89	0.015	1.42	0.032	3.02
Normal 2	270	1.028	0.010	0.97	0.016	1.56	0.000	0.00	0.020	1.95	0.015	1.46	0.032	3.11
VKA 2≤INR≤3	270	2.352	0.039	1.66	0.082	3.49	0.000	0.00	0.088	3.74	0.088	3.74	0.154	6.55
VKA 3<INR≤4	270	3.567	0.048	1.35	0.088	2.47	0.000	0.00	0.145	4.06	0.091	2.55	0.198	5.55
VKA INR>4.5	270	5.183	0.068	1.31	0.117	2.26	0.014	0.27	0.204	3.94	0.105	2.03	0.267	5.15
VKA INR>4.5	270	5.855	0.108	1.84	0.183	3.13	0.000	0.00	0.293	5.00	0.215	3.67	0.421	7.19
^CCN+	270	1.101	0.012	1.09	0.018	1.63	0.000	0.00	0.023	2.09	0.021	1.91	0.038	3.45

*SCN: STA – System Control N, SCP: STA– System Control P, Normal and Abnormal Control Materials
^CCN+ : STA – Coag Control N Plus, CCABN+ : Coag Control ABN Plus, Normal and Abnormal Control Materials

2. Linearity:

Not applicable

3. Analytical Specificity/Interference:

In the interference studies, a total of four samples (patient sample within normal reference range, VKA patient samples with $2 \leq INR \leq 3$, VKA patient samples with $3.1 \leq INR \leq 4.5$ and Deficient V patient sample) were evaluated in triplicate with three lots of STA - NeoPTimal reagent, on the STA-R family, STA Compact family and STA Satellite instrumentation on pair of plasma samples consisting of a control and a test sample. The common exogenous and endogenous interfering substances and their interference results are listed below and showed no significant interference up to the indicated concentration for all samples tested.

Interferent	Highest Concentration with No Interference
Hemoglobin	4000 mg/dL
Conjugated Bilirubin	29 mg/dL
Unconjugated Bilirubin	20 mg/dL
Triglycerides	3270 mg/dL
Unfractionated Heparin (UFH)	1.0 IU/mL
Low Molecular Weight Heparin (LMWH)	1.5 IU anti Xa/mL
Apixaban	13 ng/mL
Dabigatran	3 ng/mL
Rivaroxaban	7 ng/mL
Edoxaban	6 ng/mL

Daptomycin
According to the drug manufacturer, Daptomycin may artificially prolong PT and INR in patients with normal renal function for up to nine hours and for patients with renal impairment up to 28 hours. Therefore, PT or INR monitoring of patients on Daptomycin may be affected for up to 28 hours after dosing.

Extrinsic Factor Sensitivity
Factor sensitivity study was designed in accordance with the CLSI H47-A2 and the CLSI H48, 2nd Edition. The study was performed for factors II, V, VII and X using three lots of STA - NeoPTimal on STA-R family analyzers. For each of the extrinsic factors, a commercial single factor-deficient plasma was mixed with normal pool plasma up to eight dilutions. PT was determined in seconds in duplicate for each specific factor dilution. The sensitivity estimate determined is shown in the table below:

Extrinsic Factor	Mean (%)
Factor II	46%
Factor V	59%
Factor VII	55%
Factor X	65%

4. Assay Reportable Range:

   Not applicable

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   Quality Control
   The STA- System control N + P (K943518) and STA - Coag Control (N+ABN) PLUS (K120014) are used to perform quality control for the PT assay.

   Sample Stability Study

   a. At room temperature: To demonstrate that the citrated plasma samples remain stable for 24 hours (h) when stored at room temperature, four normal patient samples and eight VKA samples with INR between 1.5–5.5 were tested in triplicate with one lot of STA - NeoPTimal on the STA-R family of analyzers. Samples were tested at time points: 0 h, 6

h, 8 h, 21 h, 24 h and 25 h. The results support a plasma stability claim of 24 h at room temperature (18–25 °C).

b. Long-term frozen plasma stability: The long-term frozen sample stability study was done to establish the stability of samples for testing with STA - NeoPTimal and assess the stability of samples under intended storage conditions as recommended in CLSI H21-A5. A total of 53 citrated plasma samples (19 normal patient samples and 24 VKA samples with INR between 1.5–5.0) were tested in triplicate with STA - NeoPTimal on one STA-R family analyzer. Samples were tested fresh (T=0) and then frozen at -80°C. The frozen sample stability at -80°C was tested at different time points (2, 7, 8, 12 and 20 months). Data support a frozen plasma stability claim of 12 months at -80°C.

Reagent Stability Study

a. Shelf-life Stability: Study was conducted according to CLSI EP25-A. Six lots of STA - NeoPTimal were used for the shelf-life study (three lots for the 5 mL kit and three lots for the 10 mL kit). Both quality control and 3.2% citrated plasma samples were tested at different time points in triplicate on STA-R Evolution. Six timepoints were tested (0, 6, 12, 18, 24 and 25 months). Each sample was tested at each time point with three different vials of each lot of STA - NeoPTimal in triplicate. The results support a 24-month shelf-life claim at 2–8°C.

b. In-Use Stability: To assess the in-use stability of the STA - NeoPTimal, the study was performed with three lots of STA - NeoPTimal representing the two different volume configurations (5 mL and 10 mL) on the STA-R family, STA Compact family and STA Satellite instrumentation. To assess the stability of STA - NeoPTimal at 2–8°C, three lots of reagents were tested on STA-R analyzer. Testing was performed on six samples:
   - Patient sample included in the normal reference range (Normal)
   - VKA patient sample with an INR between 2.0 and 3.0 (VKA 2–3)
   - VKA patient sample with an INR between 3.1 and 4.5 (VKA 3–4.5)
   - Deficient patient sample (Def V)
   - Two controls

   All samples were tested after reconstitution in triplicate at different timepoints. The study results support the following in-use stability claim:

	STA - NeoPTimal 5 mL	**STA - NeoPTimal 10 mL**
STA-R Family, STA Compact Family	48 h on board	
STA Satellite Family	4 days on board	
2–8°C	8 days	

c. Transportation Stability Studies: The shipping study was conducted to evaluate the performance of STA - NeoPTimal throughout its claimed shelf-life when exposed to conditions experienced during transport. Two lots of STA - NeoPTimal (one for 5 mL and one for 10 mL) were subjected to simulated shipping conditions and thermal shipping stress. Each lot was stored according to specified transport conditions. After the cycle for transport condition simulation, reagents were stored unopened at 2–8°C. At different time points (0, 6, 12, 18, 24 and 25 months), the reagents were reconstituted and PT was

performed (results expressed as seconds, and INR for normal and VKA samples) on different samples in triplicate. The results demonstrate transport stability of STA - NeoPTimal under stress conditions.

6. Detection Limit:

   Not applicable

7. Assay Cut-Off:

   Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

   The method comparison study was performed for both Prothrombin Time (PT) in seconds and INR at three sites. Samples were collected in 3.2% sodium citrate and assayed in parallel and in random order on both the candidate and predicate device. At each site, one analyzer per family was used for analysis with three lots of reagents. A total of 683 patient samples were included in data analysis. The results were evaluated using a Passing-Bablok regression analysis for each site and all sites combined. The results are summarized in the following tables:

   Passing-Bablok regression analyses for all sites combined

	N	Range	Slope (95% CI)	Intercept (95% CI)	Pearson (r)
PT (Seconds)	683	10.3–95.9	1.07 (1.05, 1.09)	0.16 (-0.14, 0.46)	0.967
INR	683	0.78–7.62	0.93 (0.92, 0.95)	0.04 (0.02, 0.06)	0.965

2. Matrix Comparison:

   The sample matrix comparison studies were performed to determine the effect of freezing plasma samples on the PT test. The comparability of results for samples tested fresh and after one week of storage at -80ºC (fresh vs frozen) was assessed. Each sample was tested using one lot of STA - NeoPTimal on one analyzer of the STA-R family. A total of 40 patient samples were tested in duplicate. Specifically, 15 patient samples in the normal reference range and 25 VKA patient samples. Results in both INR and PT (seconds) met the acceptance criteria, demonstrating the STA - NeoPTimal reports comparable results on fresh and frozen plasma samples.

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable

2. Clinical Specificity:

Not applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

The study was conducted to determine the reference range of STA - NeoPTimal for PT in seconds and INR. The reference interval study was performed at three sites with a total of 137 reference samples obtained from apparently healthy individuals > 21 years of age. The reference range of STA - NeoPTimal was calculated in accordance with the CLSI EP28-A3c, as shown in the following table.

Test (units)	2.5% percentiles (95% CI)	97.5% percentiles (95% CI)
PT (seconds)	11.8 (11.6, 11.9)	14.9 (14.7, 15.3)
INR	0.89 (0.88, 0.90)	1.11 (1.10, 1.14)

F Other Supportive Instrument Performance Characteristics Data:

Instrument Family Comparison Study

An instrument family comparison study between STA analyzer families was conducted to validate that there is no significant difference within each family of analyzers; namely, the STA-R Family and the STA Compact Family. The STA-R family contains STA-R, STA-R Evolution and STA R Max. The STA Compact family contains STA Compact and STA Compact Max. Two studies were conducted, one study to compare the STA-R Evolution and STA-R Max and another to compare the STA Compact and STA Compact Max. Frozen citrated plasma samples (n=108 for STA-R and STA R Max, n=107 for STA Compact and STA Compact Max) were tested using one lot of STA - NeoPTimal on STA-R Evolution, STA-R Max, STA Compact and STA Compact Max. All results met the acceptance criteria and no significant difference for PT in seconds and INR values was observed within the same family of analyzers.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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