nanōmix eLab®

S1 Panel Cartridge
Package Insert

INTENDED USE

Nanomix S1 Panel Cartridge is a wholly contained, disposable cartridge that contains the reagents and biosensors that are used to quantitatively measure two biomarkers, C-reactive protein (CRP), and Procalcitonin (PCT) and the metabolite Lactate (LAC) in lithium heparinized (Li-heparinized) plasma and lithium heparinized venous whole blood specimens.

C - reactive protein

The Nanomix CRP assay is intended for the quantitative determination of C-reactive protein (CRP) in Li-heparinized plasma and whole blood specimens for use in a clinical or point of care (POC) location. CRP test results aid in the evaluation of infection, tissue injury, and inflammatory disorders in conjunction with other laboratory and clinical findings. CRP results are not intended for high sensitivity CRP measurement.

Procalcitonin

The Nanomix PCT assay is intended for the quantitative determination of Procalcitonin (PCT) in Li-heparinized plasma and venous whole blood specimens. Used in conjunction with other laboratory findings and clinical assessments, the PCT test results are intended for use:

- To aid in the risk assessment of critically ill patients on their first day of ICU admission for progression of severe sepsis and septic shock.
- To aid in assessing the cumulative 28-day risk of all-cause mortality for patients diagnosed with sever sepsis or septic shock in the ICU or when obtained in the emergency department of other medical wards prior to ICU admission, using a change in PCT level over time.
- To aid in decision making on antibiotic therapy for patient with suspected or confirmed lower respiratory tract infections (LRTI) defined as community acquired pneumonia (CAP) acute bronchitis, and acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in an inpatient setting or Emergency Department.
- To aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.

Lactate

The Nanomix LAC assay is intended for the quantitative determination of Lactate (LAC) in Li-heparinized plasma and venous whole blood specimens for use in a clinical or point of care location. LAC test results are used in the diagnosis and treatment of lactic acidosis, monitoring tissue hypoxia, and diagnosis of hyperlactatemia and septicemia.

All three assays (CRP, PCT and LAC) are provided on one single S1 Panel Cartridge. The results of the three assays are not intended to be combined or used together in any fashion. The S1 Panel Cartridge should only be used with the Nanōmix eLab® Analyzer. The eLab system (the analyzer and cartridge) is intended for use in clinical laboratory or POC settings.

TEST SUMMARY

The CRP and PCT biomarkers are measured using Enzyme-Linked Immuno-sorbent Assay (ELISA) methods. LAC is detected using an enzymatic method.

Antibodies are deposited on separate electrochemical sensors fabricated on a polyethylene-terephthalate (PET) substrate. Target-specific reporter-horse radish peroxidase (HRP) conjugates (CRP and PCT) are provided on an absorbent pad in a chamber upstream of the electrochemical sensors. The LAC enzyme is deposited directly on the sensor. The sample rehydrates the reporter pad before coming in contact with the capture antibodies. The sample is incubated in the detection chamber, and LAC is measured. After incubation, the sample and excess reporter are removed using an on-board wash solution. The final step is the addition of the HRP enzyme substrate, which leads to an electrochemically active product. The electronic signal detected by each electrochemical sensor is converted into a clinical unit of measurement by the eLab Analyzer using a cartridge lot-specific calibration curve.

CONTENTS

One box contains 25 cartridges inside their individually sealed pouches.

One pouch contains one single use cartridge, one 150µL pipette, and one desiccant bag (to be disposed upon opening the foil pouch).

The cartridge consists of sensors and necessary reagents to detect CRP, PCT and LAC as well as on board buffers and preservatives.

A list of biological and reactive ingredients is indicated below, Table 1.

Table 1

Reactive Ingredient	Biological Source	Quantity
IgG	Mouse IgG; Goat IgG	975 ng; 0.3 ng
Lactate oxidase	Microorganism(s)	60 µg
Azure B	N/A	2.76 µg
IgG – Peroxidase Conjugate	Mouse IgG; unspecified Peroxidase	228 ng
CRP-Peroxidase Conjugate	Human CRP; Horseradish Peroxidase	76 ng
3,3',5,5' Tetramethylbenzidine	N/A	260 µg

STORAGE INSTRUCTIONS

S1 Panel Cartridges should be stored inside their foil pouches at 2°C to 8°C. Cartridges inside their sealed foil pouches can be stored at ambient temperature for one week and may be used immediately after being removed from refrigeration.

SPECIMEN COLLECTION, STORAGE AND HANDLING

Samples are collected using a venous blood draw into a lithium heparin vacutainer tube. Whole blood can be applied directly into the sample collection port on the cartridge using the provided transfer pipette. Whole blood samples should be tested immediately upon collection.

Alternatively, plasma can be separated from the whole blood sample by centrifugation prior to testing. Apply separated plasma directly into the sample collection port on the cartridge using the provided transfer pipette. Separate plasma from blood within thirty minutes of collection and test for analytes within one hour of collection. Plasma samples can be stored at ≤-20°C for at least 4 months.

PRECAUTION

A. When delivering sample to S1 Panel Cartridge, do not release suction on sample pipette until it has been removed from the cartridge well.

B. Do not apply sample to S1 Panel Cartridge until prompted to do so by the on-screen prompts. After applying sample to S1 Panel Cartridge, promptly insert the cartridge into the analyzer and press the "Yes" button to start the assay. Discard the cartridge and reapply the sample to a new cartridge if a delay in time has occurred between sample application and start of assay.

C. Specimens may be infectious. Use Universal Precautions when performing assay. Proper handling and disposal methods should be established according to local, regional and national regulations. Only personnel adequately qualified and trained in the use of this assay should perform this procedure.

D. Use only supplied delivery pipette when loading sample onto cartridge.

E. Ensure S1 Panel Cartridge is placed on a level surface when loading.

F. Do not use S1 Panel Cartridge if it has visible cracks or appears to be damaged.

S1 Assay Instructions

1. Remove S1 Panel Cartridge pouch from refrigerator.
2. Power on the eLab Analyzer (if not already on). Enter user id and password.
3. Select **Start Assay** from the eLab Analyzer main screen.
4. Scan or enter the patient or sample identification when prompted by eLab Analyzer.

   IMPORTANT: To ensure patient privacy, do not use patient identifying information in the record ID.
5. Scan or enter the S1 Panel Cartridge pouch barcode when prompted by eLab Analyzer.
6. Select the correct sample type (Whole Venous Blood or Plasma) when prompted by eLab Analyzer.
7. Remove the cartridge and fixed-volume transfer pipette from the S1 Panel Cartridge pouch when ready to load sample for testing.
8. Use the transfer pipette to transfer the sample into the cartridge. Fill the pipette by firmly squeezing the pipette bulb before inserting the tip into the sample and then slowly releasing pressure on the bulb.

   Note*: Be sure to fully fill the pipette by aspirating enough sample so that some reaches the overfill reservoir of the pipette.*
9. Insert the loaded pipetted tip securely into sample port and firmly squeeze the pipette bulb to fully dispense the sample.

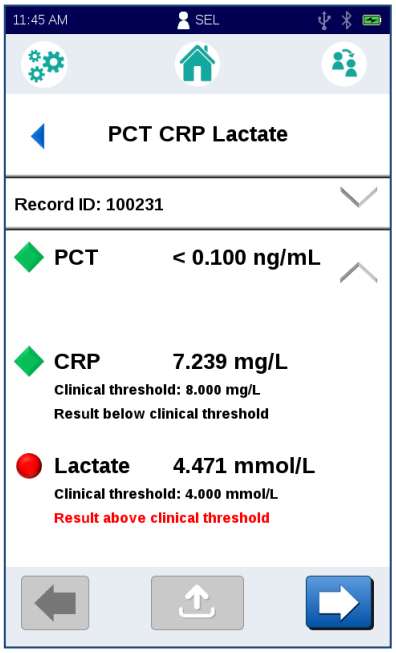
   Note*: The sample port is identified with a droplet and arrow pointing to the well.*

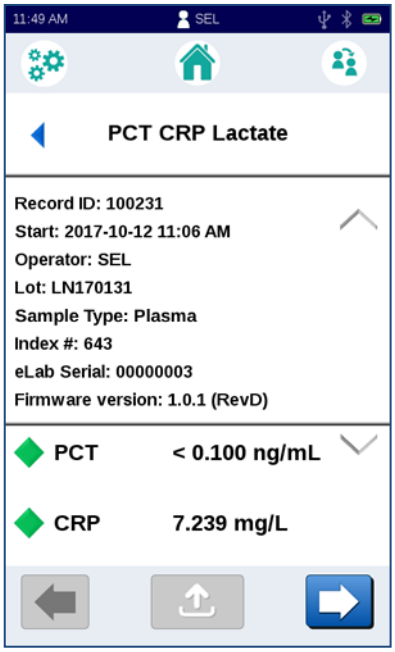
   Caution: *DO NOT release suction on transfer pipette bulb until the pipette is removed from sample port to prevent drawing the sample back out. Discard the pipette as biohazardous waste.*
10. Insert S1 Panel Cartridge into eLab Analyzer ensuring S1 Panel Cartridge clicks into seated position. The analyzer will display the **Start Assay?** screen when the cartridge is properly inserted.
11. Confirm the information (lot code, record ID and sample type) are correct, then start the assay immediately. The assay will run for approximately 12 minutes.

TEST RESULTS

Test Results Display

- Test results will appear on the screen as soon as the analyzer completes the assay.
- The Expand and Collapse arrows can be used to see more or less information.





- If reference ranges or threshold values have been enabled, a green or red symbol will be shown next to the analyte name:

◆	Result is within user configured reference range or threshold.
●	Result is outside user configured reference range or threshold.

METROLOGICAL TRACEABILITY

No user calibration is required.

Users may run quality control assays from the analyzer's Quality Control Menu. For information on commercially-available controls compatible with the S1 Panel cartridge, refer to the document S1 Panel Quality Control (PN 140129), which can be downloaded from Nanomix's website.

CLINICAL SIGNIFICANCE

CRP measurements are used for evaluation of infection, tissue injury, and inflammatory disorders.[1] CRP assays provide information for the diagnosis, therapy, and monitoring of inflammatory diseases. CRP is one of the cytokine induced "acute-phase" proteins whose blood levels rise during a general, unspecified response to infections and non-infectious inflammatory processes.[2] For conventional CRP assays, test values are typically considered to be clinically significant at levels above 10 mg/L. In healthy adult's CRP levels are below 5 mg/L. In various conditions, this threshold is often exceeded within four to eight hours after an acute inflammatory event, with CRP values reaching

approximately 20-500 mg/L.[1,3] CRP levels rise more rapidly than erythrocyte sedimentation rate (ESR), which is another indicator of acute inflammatory processes. After the disease has subsided, CRP values rapidly fall and reach the reference interval often days before ESR has returned to normal.[1,4,5]

PCT is a marker that aids in the differentiation of bacterial from viral infections.[6] Early detection of an elevated PCT level in patients with suspected bacterial infection can enable earlier antibiotic treatment.[7,8] PCT also aids in clinical decision making on when to continue or stop antibiotic therapy, improving patient care and decreasing antibiotic misuse and resistence.[9] PCT is detected in the blood stream after 3 to 4 hours in response to bacterial endotoxins and peaks at 6-8 hours with a half-life of approximately 24-30 hours.[10] It is upregulated in response to bacterial but not viral infections. The marker rises with increasing severity of infection and returns to normal as the infection resolves. In the case of bacterial infection in adults, PCT levels decrease by around 50% every 24 hours with effective antibiotic therapy. A non-decreasing level of PCT is indicative of possible treatment failure.

Elevated Lactate levels are mainly found in conditions of hypoxia such as shock, hypovolemia, and left ventricular failure; in conditions associated with diseases such as diabetes mellitus, neoplasia and liver disease; and in conditions associated with drugs or toxins such as ethanol, methanol or salicylates. An increased level of lactate in the blood is an indicator commonly used to detect tissue hypoperfusion, particularly in the case of sepsis.[11,12]

PERFORMANCE CHARACTERISTICS

Precision

Precision studies were conducted based on CLSI EP5-A3 guidelines. Three plasma samples (high, medium, low analyte levels) were tested in triplicate over 5 days at three different sites by two operators per site using one cartridge lot (N=270). A single eLab Analyzer was used at each site.

Table 3: Precision Variance Component Analysis by Analyte and Sample across All Sites and Operators

Analyte	Test Sample	N	Mean	Variance Components: SD [%CV]				
				Site/ Instrument	Operator (Site)	Day (Operator)	Repeat-ability	Total
CRP	S1	90	8.66	0.29 [3%]	0.00 [0%]	0.00 [0%]	0.91 [10%]	0.95 [11%]
	S2	88	32.52	0.00 [0%]	0.00 [0%]	1.46 [4%]	3.23 [10%]	3.54 [11%]
	S3	90	118.96	1.94 [2%]	0.00 [0%]	0.00 [0%]	13.84 [12%]	13.98 [12%]
Lactate	S1	90	1.62	0.03 [2%]	0.00 [0%]	0.00 [0%]	0.09 [6%]	0.09 [6%]
	S2	88	2.92	0.03 [1%]	0.00 [0%]	0.00 [0%]	0.29 [10%]	0.29 [10%]
	S3	90	6.49	0.00 [0%]	0.19 [3%]	0.37 [6%]	0.82 [13%]	0.92 [14%]
PCT	S1	90	0.68	0.01 [1%]	0.00 [0%]	0.02 [2%]	0.06 [10%]	0.07 [10%]
	S2	88	2.62	0.00 [0%]	0.10 [4%]	0.13 [5%]	0.24 [9%]	0.30 [11%]
	S3	90	50.52	0.00 [0%]	1.67 [3%]	1.51 [3%]	4.67 [9%]	5.18 [10%]

Other analytical and functional performance characteristics of the assay determined by testing plasma samples are summarized Table 4.

Table 4: Analytical and Functional Performance Characteristics

Assay	CRP	LAC	PCT
LOB	1.254 mg/L	0.012 mmol/L	0.026 ng/mL
LOD	1.473 mg/L	0.035 mmol/L	0.046 ng/mL
LLOQ	2.5 mg/L	0.3125 mmol/L	0.1 ng/mL
ULOQ	300 mg/L	7.5 mmol/L	220 ng/mL
Reportable Range	2.5 - 200 mg/L	0.3 - 7.5 mmol/L	0.2-200 ng/mL
Linear Range	1.25 - 300 mg/L	0.2083 - 15 mmol/L	0.2 - 220 ng/mL

A comparison of assay performance in matched whole blood and plasma samples is provided in Table 5.

Table 5: Plasma and Whole Blood Performance Comparison

	CRP (mg/L)		LAC (mM)		PCT (ng/mL)	
Sample Analyte Level	**Plasma**	**Whole Blood**	**Plasma**	**Whole Blood**	**Plasma**	**Whole Blood**
Display Range	2.5 - 200	2.5 - 50	0.2-200	0.2-200	0.3 - 7.5	0.3 - 7.5
Level 1	< 2.50	< 2.50	< 0.20	< 0.20	1.37 ± 5.0%	1.58 ± 12.4%
Level 2	4.44 ± 5.6%	4.28 ± 13.7%	0.47 ± 19.0%	0.49 ± 12.8%	1.62 ± 2.5%	1.84 ± 13.4%
Level 3	8.16 ± 23.7%	7.34 ± 22.1%	1.91 ± 10.9%	2.09 ± 17.3%	2.73 ± 4.9%	2.83 ± 10.6%
Level 4	102.89 ± 21.1%	> 50	48.47 ± 17.6%	43.15 ± 16.5%	5.68 ± 4.7%	4.97 ± 11.1%

Hematocrit Tolerance

No hematocrit effect was observed in a study of 39 paired plasma and whole blood clinical patient samples with hematocrits ranging from 23% to 53%.

Interference

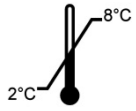
A total of 40 exogenous and endogenous substances were examined for interference effects. The table below summarizes the interference findings.

Table 6: Interference

Substance	Highest Concentration Tested		Concentration at which interference is detected*		
			PCT Assay	CRP Assay	Lactate Assay
Acetaminophen	1324	µM	ND	ND	ND
Acetylsalicylic Acid (Aspirin)	3.62	mM	ND	ND	ND
Ampicillin	152	µM	ND	ND	ND
Ascorbic acid	170	µM	ND	ND	ND
Bilirubin	342	µM	ND	ND	ND
Biotin	30	ng/mL	ND	ND	ND
Bromide	37.5	mM	ND	ND	ND
Caffeine	308	µM	ND	ND	ND
Cefepime	87.6	mg/L	ND	ND	ND
Cephalothin (Keflin)	760	µM	ND	ND	ND
Chloramphenicol	155	µM	ND	ND	ND
Dopamine	5.87	µM	ND	ND	ND
Erythromycin	81.6	µM	ND	ND	ND
Glutathione	3	mM	ND	ND	ND
Glycolic acid ^	20	mM	ND	ND	Decrease est. at >10 mM +
HAMA †	115	ng/mL	ND	Decrease est. at > 80.5 ng/mL +	ND
Hemoglobin †	2	g/L	Increase obs. at 2 g/L ‡	ND	ND
Heparin, Lithium	3000	U/L	ND	ND	ND
Heparin, Sodium	3000	U/L	ND	ND	ND
Hydroxyurea (hydroxycarbamide)	0.92	mM	ND	ND	ND
Ibuprofen	2425	µM	ND	ND	ND
Imipenem	0.5	mg/L	ND	ND	ND
Intralipid	1500	mg/dL	ND	ND	ND
Isoniazid	292	µM	ND	ND	ND
Levodopa	5	mg/dL	ND	ND	ND
Methotrexate	2	mM	ND	ND	ND
Metronidazole	701	µM	ND	ND	ND
Nafcillin	1	mg/dL	ND	ND	ND
Nitrofurantoin	16.8	µM	ND	ND	ND
Noradrenaline	2	mg/L	ND	ND	ND
Oxacillin	1	mg/dL	ND	ND	ND
Oxaloacetate ^	264	mg/dL	ND	ND	Decrease est. at > 112.5 mg/dL +
Protein (Albumin), human	60	g/L	ND	ND	ND
Pyruvate	0.31	mM	ND	ND	ND
Rheumatoid Factor	644	IU/mL	ND	Decrease est. at > 354 IU/mL ‡	ND
Rifampin	78.1	µM	ND	ND	ND
Salicylic acid	4.34	mM	ND	ND	ND
Sulfadiazine	754	µM	ND	ND	ND
Uric acid	1.4	mM	ND	ND	ND
Vncomycin	69	µM	ND	ND	ND

* ND – Not Detected: equivalent within ±30% of the control condition using a 90% confidence interval.
+ Effect only observed in high analyte concentration samples
‡ Effect only observed in low analyte concentration samples
† High concentrations of the indicated substance increases the chance of type 640 errors (internal assay controls outside limits) occurring during the S1 assay
^ Additional testing identified that glycolic acid and oxaloacetic acid have an additive effect on depressing lactate detection. Literature search suggests that combined high levels of glycolic acid/glycolate and oxaloacetic acid/oxaloacetate are very unlikely to occur in the patient population and the observed interference is most likely an artifact of the grouped screening testing scheme.

SYMBOLS

Symbol	Meaning	Title and Designation Number
CE	CE mark	Council Directive 93/68/EEC
	Consult instructions for use	ISO 15223-1, Medical devices - Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements 5.4.3, 2021 07 EN ISO 18113-1:2011 – In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) – Part 1: Terms, definitions and general requirements
	Do not re-use	ISO 15223-1, Medical devices - Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements 5.4.3, 2021 07 EN ISO 18113-1:2011 – In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) – Part 1: Terms, definitions and general requirements
	Biological risks	ISO 15223-1, Medical devices - Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements 5.4.3, 2021 07 EN ISO 18113-1:2011 – In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) – Part 1: Terms, definitions and general requirements
	Temperature limitation: Store at 2 to 8°C	ISO 15223-1, Medical devices - Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements 5.4.3, 2021 07 EN ISO 18113-1:2011 – In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) – Part 1: Terms, definitions and general requirements
IVD	In vitro diagnostic medical device	ISO 15223-1, Medical devices - Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements 5.4.3, 2021 07 EN ISO 18113-1:2011 – In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) – Part 1: Terms, definitions and general requirements
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	Expiration date	ISO 15223-1, Medical devices - Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements 5.4.3, 2021 07 EN ISO 18113-1:2011 – In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) – Part 1: Terms, definitions and general requirements
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EC REP	Authorized representative in the European community	EN ISO 18113-1:2011 – In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) – Part 1: Terms, definitions and general requirements
LOT	Lot code	ISO 15223-1, Medical devices - Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements 5.4.3, 2021 07 EN ISO 18113-1:2011 – In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) – Part 1: Terms, definitions and general requirements
	Contains <n> tests	Council Directive 93/68/EEC
	Prescription use only	21CFR801.109 PART Labeling Subpart D - Exemptions from Adequate Directions for Use. Prescription devices.

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Or login to the support page at www.nanomixsupport.com

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