BECKMAN COULTER

ACCESS
Immunoassay Systems

Instructions For Use

Access IL-6
Interleukin-6

REF A30945

For Use Under the Emergency Use Authorization (EUA) Only

For *In Vitro* Diagnostic Use

Rx Only

FOR USE ON ACCESS FAMILY OF IMMUNOASSAY SYSTEMS:
Access 2, UniCel DxC 600i, UniCel DxI 600, UniCel DxI 800, UniCel DxC 880i, UniCel DxC 860i, UniCel DxC 680i, UniCel DxC 660i

ANNUAL REVIEW

Reviewed by	Date	Reviewed by	Date

PRINCIPLE

WARNING

- This test has not been FDA cleared or approved;
- This test has been authorized by FDA under an EUA for use by authorized laboratories;
- This test has been authorized only to assist in identifying severe inflammatory response, when used as an aid in determining the risk of intubation with mechanical ventilation in confirmed COVID-19 patients; and
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of medical devices under Section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C § 360bbb- 3(b)(1), unless the authorization is terminated or revoked sooner.

CAUTION

For U.S.A. only, Federal law restricts this device to sale and distribution by or on the order of a physician, or to a clinical laboratory; and use is restricted to by or on the order of a physician.

INTENDED USE

The Access IL-6 assay is an *in vitro* diagnostic test for the quantitative measurement of IL-6 (Interleukin 6) in human serum and plasma (heparin). This assay is used to assist in identifying severe inflammatory response in patients with confirmed COVID-19 illness to aid in determining the risk of intubation with mechanical ventilation, in conjunction with clinical findings and the results of other laboratory testing.

Normal IL-6 results do not preclude development of a severe inflammatory response, and IL-6 should not be used as the sole basis for patient management decisions. Results must be combined with clinical observations, patient history, other laboratory parameters, and epidemiological information.

The Access IL-6 assay is a paramagnetic particle, chemiluminescent immunoassay and is intended for use on Access immunoassay analyzers.

The Access IL-6 immunoassay is only for use under the Food and Drug Administration's Emergency Use Authorization. For use by health care providers. For prescription use only. For *in vitro* diagnostic use only.

Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate or high complexity tests.

METHODOLOGY

The Access IL-6 assay is a simultaneous one-step immunoenzymatic ("sandwich") assay. A patient sample is added to a reaction vessel along with the paramagnetic particles coated with mouse monoclonal anti-human IL-6, blocking reagent and the alkaline phosphatase conjugate.

After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of IL-6 in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve.

SPECIMEN

SPECIMEN COLLECTION AND PREPARATION

1. Serum and plasma (heparin) are the recommended samples.
2. Observe the following recommendations for handling, processing, and storing blood samples:[1]
   - Collect all blood samples observing routine precautions for venipuncture.
   - Allow serum samples to clot completely before centrifugation.
   - Keep tubes stoppered at all times.
   - Physically separate serum or plasma from contact with cells as soon as possible.
   - Store samples tightly stoppered at room temperature (15 to 30°C) for no longer than eight hours.
   - If the assay will not be completed within eight hours, refrigerate the samples at 2 to 8°C.
   - If the assay will not be completed within 48 hours, or for shipment of samples, freeze at -20°C or colder.
   - Thaw samples only once.
3. Use the following guidelines when preparing specimens:
   - Ensure residual fibrin and cellular matter have been removed prior to analysis.
   - Follow blood collection tube manufacturer's recommendations for centrifugation.
   - Centrifuge all thawed samples prior to analysis.

4. Each laboratory should determine the acceptability of its own blood collection tubes and serum separation products. Variations in these products may exist between manufacturers and, at times, from lot-to-lot.
5. Avoid assaying lipemic/hemolyzed samples.

EQUIPMENT AND MATERIALS

REAGENTS

PRODUCT INFORMATION

Access IL-6 Reagent Pack

Cat. No. A30945: 100 determinations, 2 packs, 50 tests/pack

- Provided ready to use.
- Store upright and refrigerate at 2 to 10°C.
- Refrigerate at 2 to 10°C for a minimum of two hours before use on the instrument.
- Stable until the expiration date stated on the label when stored at 2 to 10°C.
- Stable at 2 to 10°C for 28 days after initial use.
- Signs of possible deterioration are a broken elastomeric layer on the pack or control values out of range.
- If the reagent pack is damaged (i.e., broken elastomer), discard the pack.
- All antisera are polyclonal unless otherwise indicated.

R1a:	Paramagnetic particles coated with goat anti-mouse IgG: mouse anti-human IL-6 monoclonal antibody, BSA, surfactant, < 0.1% sodium azide and 0.17% ProClin* 300
R1b:	TRIS saline buffer, proteins (porcine, goat, bovine, mouse), surfactant, < 0.1% sodium azide and 0.17% ProClin 300.
R1c:	Goat anti-human IL-6 alkaline phosphatase (bovine) conjugate, BSA, surfactant, < 0.1% sodium azide and 0.17% ProClin 300.

*ProClin™ is a trademark of The Dow Chemical Company (“Dow”) or an affiliated company of Dow.

WARNING AND PRECAUTIONS

- For *in vitro* diagnostic use.
- Patient samples and blood-derived products may be routinely processed with minimum risk using the procedure described. However, handle these products as potentially infectious according to universal precautions and good clinical laboratory practices, regardless of their origin, treatment, or prior certification. Use an appropriate disinfectant for decontamination. Store and dispose of these materials and their containers in accordance with local regulations and guidelines.
- For hazards presented by the product refer to the following sections: REACTIVE INGREDIENTS and GHS HAZARD CLASSIFICATION.

REACTIVE INGREDIENTS

> ⚠ **CAUTION**
>
> **Sodium azide preservative may form explosive compounds in metal drain lines. See NIOSH Bulletin: Explosive Azide Hazard (8/16/76).**
> **To avoid the possible build-up of azide compounds, flush wastepipes with water after the disposal of undiluted reagent. Sodium azide disposal must be in accordance with appropriate local regulations.**

GHS HAZARD CLASSIFICATION

Paramagnetic Particles (Compartment R1a)	WARNING	
		
	H317	May cause an allergic skin reaction.
	H412	Harmful to aquatic life with long lasting effects.
	P273	Avoid release to the environment.
	P280	Wear protective gloves, protective clothing and eye/face protection.
	P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
	P362+P364	Take off contaminated clothing and wash it before use.
		reaction mass of: 5-chloro-2-methyl-4-isothiazolin -3-one [EC# 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC# 220-239-6](3:1) < 0.05%
Blocking Agent (Compartment R1b)	WARNING	
		
	H317	May cause an allergic skin reaction.
	H412	Harmful to aquatic life with long lasting effects.
	P273	Avoid release to the environment.
	P280	Wear protective gloves, protective clothing and eye/face protection.
	P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
	P362+P364	Take off contaminated clothing and wash it before use.
		reaction mass of: 5-chloro-2-methyl-4-isothiazolin -3-one [EC# 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC# 220-239-6](3:1) < 0.05%
Conjugate (Compartment R1c)	WARNING	

H317	May cause an allergic skin reaction.
H412	Harmful to aquatic life with long lasting effects.
P273	Avoid release to the environment.
P280	Wear protective gloves, protective clothing and eye/face protection.
P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
P362+P364	Take off contaminated clothing and wash it before use.
	reaction mass of: 5-chloro-2-methyl-4-isothiazolin -3-one [EC# 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC# 220-239-6](3:1) < 0.05%

SDS	Safety Data Sheet is available at beckmancoulter.com/techdocs

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

1. Access IL-6 Calibrators
   Provided at zero and approximately 2.5, 25, 250, 750 and 1,500 pg/mL.
   Cat. No. A30944
2. Access IL-6 Quality Control (QC) or other commercially available control material.
   Provided at approximately 8.0, 300 and 800 pg/mL.
   Cat. No. A30946
3. Access Sample Diluent A
   Vial Cat. No. 81908
   Diluent Pack Cat. No. A79783 (For use with the UniCel DxI system onboard dilution feature.)
4. Access Substrate
   Cat. No. 81906
5. **Access 2, UniCel DxC 600i:**
   Access Wash Buffer II, Cat. No. A16792
   UniCel DxI 600, UniCel DxI 800, UniCel DxC 880i, UniCel DxC 860i, UniCel DxC 680i, UniCel DxC 660i:
   UniCel DxI Wash Buffer II, Cat. No. A16793

CALIBRATION

CALIBRATION INFORMATION

An active calibration curve is required for all tests. For the Access IL-6 assay, calibration is required every 28 days. Refer to the appropriate system manuals and/or Help system for information on calibration theory, configuring calibrators, calibrator test request entry, and reviewing calibration data.

TRACEABILITY

The measurand (analyte) in the Access IL-6 Calibrators is traceable to the manufacturer's working calibrators. Traceability process is based on EN ISO 17511.

The assigned values were established using representative samples from this lot of calibrator and are specific to the assay methodologies of the Access reagents. Values assigned by other methodologies may be different. Such differences, if present, may be caused by inter-method bias.

The NIBSC/WHO International Standard for IL-6 (89/548) which was intended as a potency standard, was evaluated in the kit. The NIBSC/WHO standard is a CHO cell-derived recombinant human IL-6. The dose response curve of the International Standard (89/548) parallels the Access IL-6 calibration curve. To convert sample values obtained with the Access IL-6 kit to equivalent NIBSC 89/548 units, use the following equation:

NIBSC (89/548) equivalent value (IU/mL) = 0.107 x Access IL-6 value (pg/mL)

QUALITY CONTROL

Quality control materials simulate the characteristics of patient samples and are essential for monitoring the system performance of immunochemical assays. Because samples can be processed at any time in a “random access” format rather than a “batch” format, quality control materials should be included in each 24-hour time period.[2] Include Access IL-6 QC or other commercially available quality control materials that cover at least two levels of analyte. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws. Follow manufacturer's instructions for reconstitution and storage. Each laboratory should establish mean values and acceptable ranges to assure proper performance. Quality control results that do not fall within acceptable ranges may indicate invalid test results. Examine all test results generated since obtaining the last acceptable quality control test point for this analyte. Refer to the appropriate system manuals and/or Help system for information about reviewing quality control results.

TESTING PROCEDURE(S)

PROCEDURAL COMMENTS

1. Refer to the appropriate system manuals and/or Help system for a specific description of installation, start-up, principles of operation, system performance characteristics, operating instructions, calibration procedures, operational limitations and precautions, hazards, maintenance, and troubleshooting.
2. Mix contents of new (unpunctured) reagent packs by gently inverting pack several times before loading on the instrument. Do not invert open (punctured) packs.
3. Use one hundred ten (110) µL of patient sample for each determination, in addition to the sample container and system dead volumes, when requesting the IL-6 assay (test name: IL-6), or when running with the onboard dilution feature (test name: dIL-6) on UniCel DxI 600, UniCel DxI 800, UniCel DxC 880i, UniCel DxC 860i, UniCel DxC 680i, and UniCel DxC 660i. Refer to the appropriate system manuals and/or Help system for the minimum sample volume required.
4. The system default unit of measure for sample results is pg/mL. To change sample reporting units to the International System of Units (SI units), IU/mL, refer to the appropriate system manuals and/or Help system. To manually convert concentrations to the International System, multiply pg/mL by multiplication factor 0.107.

PROCEDURE

Refer to the appropriate system manuals and/or Help system for information on managing samples, configuring tests, requesting tests, and reviewing test results.

RESULTS INTERPRETATION

Patient test results are determined automatically by the system software using a weighted four parameter logistic curve (4PLC) math model. The amount of analyte in the sample is determined from the measured light production by means of the stored calibration data. Patient test results can be reviewed using the appropriate screen. Refer to the appropriate system manuals and/or Help system for complete instructions on reviewing sample results.

REPORTING RESULTS

EXPECTED RESULTS

1. Each laboratory should establish its own reference ranges to assure proper representation of specific populations.
2. Serum samples were obtained from 151 apparently healthy individuals and analyzed with the Access IL-6 assay. According to a non-parametric reference interval analysis, the IL-6 upper 95% interval of the reference range is < 6.4 pg/mL with a 95% confidence interval (CI) of 5.3-7.5 pg/mL.

Age Range (years)	n	IL-6 Upper 95% Interval (pg/mL)	95% CI (pg/mL)
22-73	151	< 6.4	5.3-7.5

PROCEDURAL NOTES

LIMITATIONS

1. Samples can be accurately measured within the analytic range of the assay (2 pg/mL to ~1,500 pg/mL).
   - If a sample contains less than the lower limit of quantitation (LoQ) for the assay, report the results as less than that value (i.e., < 2 pg/mL).
   - If a sample contains more than the stated value of the highest Access IL-6 Calibrator (S5), report the result as greater than that value (i.e., > 1,500 pg/mL). Alternatively, use one of the dilution options below:

     Onboard Dilution Feature for use on UniCel DxI 600, UniCel DxI 800, UniCel DxC 880i, UniCel DxC 860i, UniCel DxC 680i, and UniCel DxC 660i:

     Samples containing IL-6 concentrations greater than the concentration of the Access IL-6 S5 calibrator can be processed using the UniCel DxI Onboard Dilution Feature (test name **dIL-6**.) The feature uses one volume of sample with two volumes of Access Sample Diluent which allows sample quantitation of up to approximately 4,500 pg/mL. Refer to the appropriate system manuals and/or Help system for instructions on entering a sample dilution in a test request. The system reports the results adjusted for the dilution.

Test Name	Reportable Range (pg/mL)	Sample Volume Required
IL-6	2 - 1500	110 µL
dIL-6 (Onboard dilution)	1275 - 4500	110 µL

Manual dilution:

Dilute one volume of sample with two volumes of Access IL-6 Calibrator S0 (zero) or Access Sample Diluent A.

2. For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or have received immunotherapy or diagnostic procedures utilizing immunoglobulins or immunoglobulin fragments may produce antibodies, e.g. HAMA, that interfere with immunoassays. Additionally, other heterophile antibodies such as human anti-goat antibodies may be present in patient samples.[3,4] Such interfering antibodies may cause erroneous results.
3. Other potential interferences such as rheumatoid factor (RF) in the patient sample may cause erroneous results in immunoassays. Carefully evaluate results if the sample is suspected of having RF interference.

4. The Access IL-6 results should be interpreted in light of the total clinical presentation of the patient, including: symptoms, clinical history, data from additional tests, and other appropriate information.
5. The Access IL-6 assay does not demonstrate any “hook” effect up to 30,000 pg/mL.

Conditions of Authorization for the Laboratory

The Access IL-6 assay Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, and authorized labeling are available on the FDA website: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.
However, to assist clinical laboratories using the Access IL-6 assay (“your product” in the conditions below), the relevant Conditions of Authorization are listed below:

- Authorized laboratories (c) using your product will include with result reports of your product, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- Authorized laboratories using your product will use your product as outlined in the Instructions for Use. Deviations from the authorized procedures, including the authorized instruments, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.
- Authorized laboratories using your product will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- Authorized laboratories will collect information on the performance of your product and report to DIHD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and Beckman Coulter Inc. or https://www.beckmancoulter.com or (800) 524-3633 for any suspected occurrence of false reactive or false non-reactive results and significant deviations from the established performance characteristics of your product of which they become aware.
- All laboratory personnel using your product must be appropriately trained in automated immunoassay techniques and use appropriate laboratory and personal protective equipment when handling this kit and use your product in accordance with the authorized labeling. All laboratory personnel using the assay must also be trained in and be familiar with the interpretation of results of the product.
- Beckman Coulter, Inc., authorized distributors, and authorized laboratories using your product will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

(c) The letter of authorization refers to, “Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate or high complexity tests” as “authorized laboratories".

PERFORMANCE CHARACTERISTICS

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DILUTION RECOVERY

Serial dilutions of two serum samples containing various spiked recombinant human IL-6 levels were diluted with Access IL-6 Calibrator S0 (zero) and run on the Access Immunoassay System. This study resulted in the following data:

Sample 1	Expected Concentration (pg/mL)	Determined Concentration (pg/mL)	Recovery (%)
Neat	-	1,325.0	-
1:2	662.5	678.0	102

Sample 1	Expected Concentration (pg/mL)	Determined Concentration (pg/mL)	Recovery (%)
1:4	331.3	341.0	103
1:8	165.6	180.1	109
1:16	82.8	93.0	112
1:32	41.4	47.0	114
1:64	20.7	23.4	113
1:128	10.4	11.9	115
1:256	5.2	5.5	106
1:512	2.6	2.9	112
1:1024	1.3	1.5	116
		Mean % Recovery	**110**

Sample 2	Expected Concentration (pg/mL)	Determined Concentration (pg/mL)	Recovery (%)
Neat	-	1,376.0	-
1:2	688.0	693.0	101
1:4	344.0	360.0	105
1:8	172.0	182.0	106
1:16	86.0	95.0	110
1:32	43.0	48.0	112
1:64	21.5	25.0	116
1:128	10.8	12.0	112
1:256	5.4	5.9	110
1:512	2.7	2.9	108
1:1024	1.3	1.4	104
		Mean % Recovery	**108**

LINEARITY

The Access IL-6 assay demonstrates acceptable linearity throughout the analytical measuring range of 2 to 1,500 pg/mL. Three serum and three lithium heparin samples containing IL-6 levels from below 2 pg/mL to above 1,500 pg/mL were diluted with Access IL-6 S0 calibrator and run on the Access and Access 2 Immunoassay Systems. The following tables summarize the results of the linear regression analysis based upon the CLSI EP06-A guideline.[5]

Lithium Heparin Plasma

Sample	Range (pg/mL)	Slope		Intercept		R^2	% Recovery Range
		Point Estimate	(95% CI)	Point Estimate	(95% CI)		
1	1.3 – 1555.4	1.04	(1.03 – 1.06)	-0.246	(-0.319 – -0.173)	1.000	88% - 107%
2	1.6 - 1512.9	0.98	(0.95 - 1.01)	0.064	(-0.056 – 0.185)	0.999	94% - 107%
3	1.6 - 1591.2	1.02	(1.007 - 1.04)	0.064	(-0.008 – 0.135)	1.000	98% - 108%

Serum

Sample	Range (pg/mL)	Slope		Intercept		R^2	% Recovery Range
		Point Estimate	(95% CI)	Point Estimate	(95% CI)		
1	1.3 - 1540.8	1.003	(0.98 - 1.02)	-0.243	(-0.329 – -0.156)	0.999	85% - 105%
2	1.3 – 1503.7	1.04	(1.02 – 1.06)	-0.257	(-0.336 – -0.177)	0.999	87% - 107%
3	1.6 – 1596.2	1.01	(0.97 – 1.05)	0.024	(-0.145 – 0.193)	0.998	96% - 107%

*Analysis demonstrated no significant deviation from linearity following EP06-A.

IMPRECISION

This assay exhibits total imprecision < 12% at concentrations greater than 2 pg/mL. One study run on the DxI 800 Immunoassay system, using ten serum samples across the measuring range generating a total of 10 assays, 2 replicates per assay, over 5 days provided the following data, analyzed via analysis of variance (ANOVA).[6,7] This study also included three quality control (QC) samples run once per day in duplicate.

		Within-Run (Repeatability)		Within Laboratory (Total)	
Sample	Mean (pg/mL)	SD (pg/mL)	CV	SD (pg/mL)	CV
1	3	0.3	8%	0.3	9%
2	10	0.4	4%	0.7	7%
3	26	0.6	2%	1.3	5%
4	18	0.8	4%	1.1	6%
5	70	1.0	1%	2.5	4%
6	137	2.6	2%	7.0	5%
7	286	6.4	2%	10.2	4%
8	518	8.9	2%	18.3	4%
9	792	14.5	2%	26.3	3%

		Within-Run (Repeatability)		Within Laboratory (Total)	
Sample	**Mean (pg/mL)**	**SD (pg/mL)**	**CV**	**SD (pg/mL)**	**CV**
10	1121	28.0	3%	40.0	4%
QC1	7	0.2	2%	0.3	4%
QC2	281	1.5	1%	7.8	3%
QC3	733	24.7	3%	24.7	3%

ANALYTICAL SPECIFICITY / INTERFERENCES

Samples containing up to 500 mg/dL of hemoglobin, 40 mg/dL bilirubin, 3,000 mg/dL triglycerides, 3,000 mg/dL protein (human serum albumin), 8,000 units/dL heparin, 20 mg/dL acetaminophen, 50 mg/dL acetylsalicylic acid, 40 mg/dL ibuprofen, 400 mg/dL α-2-Macroglobulin, 200 mg/dL α-1-Antitrypsin, 5 g/dL γ-globulins, and 1:20 dilution of multi-vitamin do not affect the concentration of IL-6 assayed.

The following table describes the cross-reactivity of the assay with substances that are similar in structure to IL-6 tested with IL-6 concentration of approximately 10 pg/mL on the Access and Access 2 Immunoassay systems.

Substance	**Analyte Added (pg/mL)**	**Cross-reactivity (% by weight)**
G-CSF	50,000	0.0002
Soluble IL-6 receptor (IL-6sR)	50,000	-0.0002
Soluble glycoprotein 130 (sgp130)	50,000	-0.0004
IL-6sR/sgp130 complex	50,000	-0.0005
IL-1α	50,000	0.0056
IL-1β	50,000	0.0056
IL-2	50,000	0.0056
IL-4	50,000	0.0002
IL-8	50,000	0.0024
TNF-α	50,000	0.0002

Note: All substances listed are recombinant human proteins.

ANALYTICAL SENSITIVITY

Limit of Blank (LoB), Limit of Detection (LoD), Limit of Quantitation (LoQ) were tested following CLSI EP17-A2 on the Access 2 Immunoassay system.[8]

- The Limit of Blank (LoB) is the 95th percentile from n ≥ 60 measurements of analyte-free samples. The Limit of Blank corresponds to the concentration below which analyte-free samples are observed with a probability of 95%.
- The Limit of Detection (LoD) was determined based on the LoB and the standard deviation of low concentration samples. The Limit of Detection corresponds to the lowest analyte concentration that can be detected above the LoB with a probability of 95%.
- The Limit of Quantitation is the lowest analyte concentration that can be measured with within-laboratory imprecision %CV ≤ 20%.

The maximum observed results across the two reagent lots and the corresponding criteria are shown in the table below:

Parameter	Maximum of Observed Results (pg/mL)	Criteria (claim) (pg/mL)
Limit of Blank (LoB)	0.3	≤ 2
Limit of Detection (LoD)	0.6	≤ 2
Limit of Quantitation (LoQ)	0.8	≤ 2

Matrix comparison: serum vs. plasma

In addition to serum specimens, Li-heparin and Na-heparin were tested on the Access 2 Immunoassay system and found acceptable based on the criterion of slope = 1.00 ± 0.12.

Sample	Range (pg/mL)	Slope (95% CI)	y-intercept (95 % CI)	Correlation coefficient R^2
Li-heparin	0.58 - 1064	1.08 (1.02 – 1.14)	0.000 (-0.164, 0.165)	0.996
Na-heparin	0.58 – 1063	1.03 (0.99 – 1.07)	0.047 (-0.074, 0.168)	0.994

Clinical Performance

The data collection to support the Access IL-6 clinical performance claims was part of a retrospective study conducted at the University Hospital Germans Trias I Pujol (UHG), a public research center in Spain. The study enrolled adults who presented to the Emergency Department (ED) between March 18th and May 4th, 2020 with symptoms suggestive of COVID-19 and whose standard of care testing involved IL-6 and RT-PCR COVID-19 testing.

Seventy-five (75) RT-PCR confirmed SARS-CoV-2 patients were included in the clinical performance analysis. The analysis is based on the first Access IL-6 value obtained at presentation to the ED. Statistics shown in the table below were calculated based on a cutoff of 35 pg/mL and patients who had PaO2/FiO2 ratio < 150 mmHg, which is indicative of the risk for intubation with mechanical ventilation[9]. The prevalence of the PaO2/FiO2 ratio < 150 mmHg was 55% (41/75) in this cohort.The score approach was used to calculate the 95% confidence intervals.

IL-6 (pg/mL)	PaO2/FiO2 Ratio < 150 mmHg	PaO2/FiO2 Ratio ≥ 150 mmHg	Total
> 35	35	12	47
≤ 35	6	22	28
Total	41	34	75

Clinical Evaluation Statistics

	Estimate	95% Confidence Intervals	
		Lower	Upper
Sensitivity	85.4%	71.6%	93.1%
Specificity	64.7%	47.9%	78.5%
PPV	74.5%	60.5%	84.8%
NPV	78.6%	60.5%	89.8%

Cutoff Determination

The cutoff of 35 pg/mL was determined based on published literature.[9]

Results and Interpretation

PCR confirmed COVID-19 patients that have Access IL-6 concentration > 35 pg/mL at presentation are at increased risk for intubation with mechanical ventilation during their hospitalization. IL-6 values should be used in conjunction with clinical findings and the results of other laboratory parameters. IL-6 values alone are not indicative of the need for intubation or mechanical ventilation.

ADDITIONAL INFORMATION

Developed and manufactured in collaboration with R&D Systems, a Bio-Techne brand.**

REVISION HISTORY

Revision J

IFU updated for EUA release.

SYMBOLS KEY

Glossary of Symbols is available at beckmancoulter.com/techdocs (document number C02724).

REFERENCES

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