Instructions for Use

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# sInterleukin-2-Receptor ELISA

**Enzyme immunoassay for the quantitative determination of human soluble Interleukin-2 receptor (sIL-2R) in serum and plasma (EDTA, citrate, heparin).**

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Σ **96**

2°C 8°C

EU: IVD CE 2797

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## REVISION HISTORY OF INSTRUCTIONS FOR USE

New product

## 1. INTENDED USE

Enzyme immunoassay for the quantitative determination of human soluble Interleukin-2 receptor (sIL-2R) in serum and plasma (EDTA, citrate, heparin).

## 2. INTENDED PURPOSE

The sInterleukin-2-Receptor ELISA is intended for the quantitative determination of human soluble IL-2 receptor (sIL-2R) in serum and plasma (EDTA, citrate, heparin).
sIL-2R levels can be used as physiological marker for the indication of inflammation in the body, in-vivo immune system activation and response activity. As such the measurement of sIL-2R levels is applied as an aid in the diagnosis or monitoring of therapy of autoimmune diseases (e.g. sarcoidosis).
The sInterleukin-2-Receptor ELISA is a solid phase enzyme-linked immunosorbent assay (ELISA), based on the on the sandwich principle measured on an absorbance reader. The assay is semi-automated requiring general purpose laboratory instruments and consumables such as absorbance microplate reader/washer, vortexer and pipettes to execute the test. Test results may be calculated from a standard curve and compared to laboratory established reference ranges from healthy adults (i.e. normal ranges). The test kit is intended for manual use and can be adapted to different ELISA processors like EVOlyzer.
The test kit is intended for professional laboratory use by trained personnel. The test kit is not for self-testing. The sInterleukin-2-Receptor ELISA is NOT intended for near-patient testing.

## 3. SUMMARY AND EXPLANATION

The interleukin-2 Receptor (IL-2R) is composed of at least 3 distinct polypeptide subunits termed IL-2R alpha (TAC), IL-2R beta and IL-2R gamma. [1]

In 1985 the soluble Interleukin-2 Receptor (sIL-2R, sCD25, sTAC, sIL2R) was first described as being actively released by activated peripheral blood T-cells via proteolytic cleavage of the cell surface IL-2R. [2]

Increased blood levels of sIL-2R are considered as an indication of an on-going immune response which could be used to monitor immune mediated diseases.[3]

In particular conditions that are characterized by excessive production of lymphocytes, termed lymphoproliferative disorders, show high sIL-2R levels compared to healthy controls. But also granulomatous diseases, in which T-cell activation is a typical hallmark, show elevated sIL-2R levels.

Rubin and Nelson already reported in 1990 that there are no significant sex-related differences. [2] Yet, there are age dependent levels found during infancy, which decline to adult levels during teenage years and then rise again in elderly people. [4]

Measurement of sIL-2R levels is therefore useful as a diagnostic tool in diseases like sarcoidosis or common variable immunodeficiency (CVID) as a marker of disease activity or in other lymphoproliferative disorders like hemophagocytic lymphohistiocytosis (HLH) [5; 6] or autoimmune diseases characterized by T-cell activation. Elevated sIL-2R levels have been reported in numerous studies in sarcoidosis patients. [7; 8] Some studies even indicate that measurement of sIL-2R could be a marker of therapy success.[9; 10]

Several studies have shown elevated sIL-2R levels in ANCA-Associated Vasculitis (AAV), Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA). [11; 12]

## 4. TEST PRINCIPLE

Solid phase enzyme-linked immunosorbent assay (ELISA) based on the sandwich principle. The wells are coated with specific antibody directed against sIL-2R. The sIL-2R in the sample binds to the antibody coated wells and is detected by a secondary biotinylated antibody. A streptavidin enzyme conjugate catalyzes the substrate reaction. The intensity of the color developed is proportional to the amount of sIL-2R detected.

## 5. WARNINGS AND PRECAUTIONS

1. For *in-vitro diagnostic* use only. For professional use only by GLP trained professionals.
2. Before starting the assay, read the instructions completely and carefully. Use the valid version of the package insert provided with the kit. Be sure that everything is understood.
3. In case of severe damage of the kit package please contact IBL or your supplier in written form, latest one week after receiving the kit. Do not use damaged components in test runs, but keep safe for complaint related issues.
4. Broken glass may cause injury. Handle glass vessels with caution.
5. Obey lot number and expiry date. Do not mix reagents of different lots. Do not use expired reagents.
6. Follow good laboratory practice and safety guidelines. Wear lab coats, disposable latex gloves and protective glasses where necessary.
7. Reagents of this kit containing hazardous material may cause eye and skin irritations. See MATERIALS SUPPLIED and labels for details. Safety Data Sheets for this product are available on the IBL-Homepage or upon request directly from IBL.
8. Chemicals and prepared, used, unused or expired reagents have to be treated as hazardous waste according to national biohazard and safety guidelines or regulations.
9. The cleaning staff should be guided by the professionals regarding potential hazards and handling.
10. All serious incidents that have occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.
11. Avoid contact with Stop solution. It may cause irritations and burns.
12. The device contains material of animal origin, which is certified apparently free of infectious or contagious diseases and injurious parasites. Still the material should be handled with extreme caution.

## 6. STORAGE AND STABILITY

The kit is shipped at ambient temperature and should be stored at 2 - 8°C. Keep away from heat or direct sunlight. The storage and stability of specimens and prepared reagents are stated in the corresponding chapters.

The unopened reagents are stable until the expiry date indicated. The kit is stable up to 6 months after the first opening (not exceeding the expiry date) when the Microtiter plate is packed in a tightly closed bag, the bottles are closed with their screw caps and the kit is stored at indicated storage temperature.

## 7. SPECIMEN COLLECTION AND STORAGE

**Specimen**
Serum, Plasma (EDTA, Heparin, Citrate)

**Specimen collection**
The usual precautions for venipuncture should be observed. It is important to preserve the chemical integrity of a blood specimen from the moment it is collected until it is assayed. Do not use grossly hemolytic, icteric or lipemic specimens. Samples appearing turbid should be centrifuged before testing to remove any particulate material.

**Sample Collection Device**
No special requirements.

**Specimen storage**
Samples can be stored at 2 - 8°C for up to 3 days.
It is recommended to freeze samples and store at -20°C for long time storage (< 6 months).
Avoid repeated freeze-thaw cycles. It is recommended to limit the number of freeze /thaw cycles to a maximum of 3. Keep away from heat or direct sunlight.

## 8. MATERIALS SUPPLIED

| Quantity | Symbol | Origin | Component |
|---|---|---|---|
| 1 x 12 x 8 | MTP | BIO | **Microtiter Plate,** Break apart strips.<br>MTP (12 strips of 8 wells each)<br>Coated with anti-human sIL-2R (mouse monoclonal). Vacuum dried. |
| 6 x 1 x 1mL | CAL A - F | BIO | **Standard A-F,** Ready to use.<br>0; 7; 20; 40; 80; 160 U/mL<br>Contains: sIL-2R, phosphate buffer, bovine serum albumin and ≤ 0.1 % ProClin 300 (w/w). |
| 2 x 1 x 1mL | CONTROL 1<br>CONTROL 2 | BIO | **Control 1+2,** Ready to use.<br>Contains: sIL-2R, phosphate buffer, bovine serum albumin and ≤ 0.1 % ProClin 300 (w/w).<br>Concentrations / acceptable ranges see labels or QC certificate. |
| 1 x 9 mL | BIOTIN AB | BIO | **Biotinylated Antibody,** Ready to use.<br>Red colored. Contains: anti-human sIL-2R (mouse monoclonal) conjugated to biotin, phosphate buffer, bovine protein and ≤ 0.1 % ProClin 300 (w/w). Sediment must be stirred before use, vortex thoroughly and shake vigorously by hand. A turbidity may occur without influence of assay performance and test results. |
| 1 x 20 mL | SAMPLEDIL | BIO | **Sample Diluent,** Ready to use.<br>Contains: phosphate buffer, bovine protein and ≤ 0.1 % ProClin 300 (w/w). Sediment must be stirred before use, vortex thoroughly and shake vigorously by hand. A turbidity may occur without influence of assay performance and test results. |
| 1 x 15 mL | ENZCONJ | | **Enzyme Conjugate,** Ready to use.<br>Contains: streptavidin conjugated to HRP and ≤ 0.1 % ProClin 300 (w/w). |
| 1 x 100 mL | WASHBUF CONC | | **Wash Buffer,** Concentrate (10x)<br>Contains: phosphate buffer with 1 % Tween 20 (w/w). |
| 1 x 15 mL | TMB SUBS | | **TMB Substrate Solution,** Ready to use.<br>Contains: Tetramethylbenzidine. |
| 1 x 15 mL | TMB STOP | | **TMB Stop Solution,** Ready to use.<br>Contains: 0.5 M sulfuric acid. |
| 3 x | FOIL | | **Adhesive Foil** |

## 9. MATERIALS REQUIRED BUT NOT SUPPLIED

1. Micropipettes (Multipette Eppendorf or similar devices, < 3 % CV).
   Volume: 0-20 µL; 10-100 µL; 100-1000 µL
2. Vortex mixer
3. Wash bottle, automated or semi-automated microtiter plate washing system
4. Bidistilled or deionised water
5. Paper towels, pipette tips and timer
6. Microtiter plate reader capable of reading absorbance at 450 nm (reference wavelength 600 - 650 nm)
7. Tubes for sample dilution (disposable polypropylene tubes)
8. 8-Channel Micropipettor with reagent reservoirs

## 10. PROCEDURE NOTES

1. Any improper handling of samples or modification of the test procedure may influence the results. The indicated pipetting volumes, incubation times, temperatures and pre-treatment steps have to be performed strictly according to the instructions. Use calibrated pipettes and devices only.
2. Once the test has been started, all steps should be completed without interruption. Make sure that required reagents, materials and devices are prepared and ready at the appropriate time. Allow all reagents and specimens to reach room temperature (18 - 25°C) and gently swirl each vial of liquid reagent and sample before use. Mix reagents without foaming.
3. Avoid contamination of reagents, pipettes and wells/tubes. Use new disposable plastic pipette tips for each component and specimen. Do not interchange caps. Always cap not used vials. Do not reuse wells/tubes or reagents.
4. It is advised to perform duplicate measurements to be able to identify potential pipetting errors.

5. Use a pipetting scheme to verify an appropriate plate layout.
6. Incubation time affects results. All wells should be handled in the same order and time sequences. It is recommended to use an 8-channel micropipette for pipetting of solutions in all wells.
7. Microtiter plate washing is important. Improperly washed wells will give erroneous results. It is recommended to use a multichannel pipette or an automatic microtiter plate washing system. Do not allow the wells to dry between incubations. Do not scratch coated wells during rinsing and aspiration. Rinse and fill all reagents with care. While rinsing, check that all wells are filled precisely with Wash Buffer, and that there are no residues in the wells.
8. Humidity affects the coated wells/tubes. Do not open the pouch until it reaches room temperature. Unused wells/tubes should be returned immediately to the resealed pouch including the desiccant.

## 11. PRE-TEST SETUP INSTRUCTIONS

### 11.1. Preparation of concentrated components

The volumes stated below are for one run with all strips (96 determinations).

| Dilute / dissolve | Component | with | Diluent | Relation | Remarks | Storage | Stability |
|---|---|---|---|---|---|---|---|
| 100 mL | **WASHBUF CONC** | 900 mL | bidist. water | 1:10 | Mix gently, avoid foaming | 2 - 8°C | up to 30 days |

### 11.2. Dilution of Samples

Samples suspected to contain concentrations higher than the measuring range have to be diluted with Sample Diluent. Measured results must be multiplied with the dilution factor to obtain corrected results.

## 12. TEST PROCEDURE

| | |
|---|---|
| **1.** | Pipette **100 µL** of each **Standard and Control** into the respective wells of microtiter plate. |
| **2.** | Pipette **50 µL** of **Sample Diluent** into the **sample** wells of the microtiter plate. |
| **3.** | Pipette **50 µL** of **each sample** into the respective wells of the microtiter plate. |
| **4.** | Thoroughly mix for 10 seconds. |
| **5.** | Cover plate with adhesive foil and incubate microtiter plate for **2 hours at 18 - 25°C** (room temperature). |
| **6.** | Remove adhesive foil. Discard incubation solution. **Wash** plate **3x with 300 µL** of **diluted Wash Buffer**. Remove excess solution by tapping the inverted plate on a paper towel. Automatic microtiter plate washers should be adjusted to overflow mode. |
| **7.** | Pipette **50 µL** of **Biotinylated Antibody** into all wells of the microtiter plate. |
| **8.** | Cover plate with new adhesive foil and incubate microtiter plate for **1 hour at 18 - 25°C**. |
| **9.** | Remove adhesive foil. Discard incubation solution. **Wash** plate **3x with 300 µL** of **diluted Wash Buffer**. Remove excess solution by tapping the inverted plate on a paper towel. Automatic microtiter plate washers should be adjusted to overflow mode. |
| **10.** | Pipette **100 µL** of **Enzyme Conjugate** into all wells of the microtiter plate. |
| **11.** | Cover plate with new adhesive foil and incubate microtiter plate for **30 minutes at 18 - 25°C**. |
| **12.** | Remove adhesive foil. Discard incubation solution. **Wash** plate **3x with 300 µL** of **diluted Wash Buffer**. Remove excess solution by tapping the inverted plate on a paper towel. Automatic microtiter plate washers should be adjusted to overflow mode. |
| **13.** | Pipette **100 µL** of **TMB Substrate Solution** into each well. Briefly mix contents by gently shaking the plate. |
| **14.** | **Incubate** microtiter plate for **10 - 15 minutes at 18 - 25°C**. |
| **15.** | Stop the substrate reaction by adding **100 µL** of **TMB Stop Solution** into each well. Briefly mix contents by gently shaking the plate. |
| **16.** | Measure optical density with a photometer at **450 nm** (Reference-wavelength: 600 - 650 nm) within **15 minutes** after pipetting the Stop Solution. |

## 13. AUTOMATION

Automated protocols can be provided for open ELISA systems: Freedom EVOlyzer®, ThunderBolt® and DSX®. For further information please contact: ProductSupport.IBL@tecan.com

For the use of products on automated instruments it is absolutely necessary to perform and maintain a validation according to legal requirements. A successful validation of the process is a prerequisite for diagnostic use. The responsibility for the implementation and documentation of validation in accordance with the country-specific requirements is assumed by the organization or institution.

## 14. QUALITY CONTROL

The test results are only valid if the test has been performed following the instructions. Moreover, the user must strictly adhere to the rules of GLP (Good Laboratory Practice) or comparable standards/laws. User and/or laboratory must have a validated system to get diagnosis according to GLP. All kit controls must be found within the acceptable ranges as stated on the labels and the QC certificate. If the criteria are not met, the run is not valid and should be repeated. Each laboratory should use known samples as further controls.

In case of any deviation the following technical issues should be proven: Expiration dates of (prepared) reagents, storage conditions, pipettes, devices, incubation conditions and washing methods.

It is recommended to participate at appropriate quality assessment trials.

## 15. CALCULATION OF RESULTS

The obtained ODs of the standards (y-axis, linear) are plotted against their concentration (x-axis, logarithmic) either on semi-logarithmic graph paper or using an automated method. A good fit is provided with cubic spline, 4 Parameter Logistics or Logit-Log.

For the calculation of the standard curve, apply each signal of the standards (one obvious outlier of duplicates could be omitted and the more plausible single value used).

The sample dilution of 1:2 has to be taken into consideration when reading the results from the graph. The concentration read from the standard curve must be multiplied by the dilution factor (x 2).

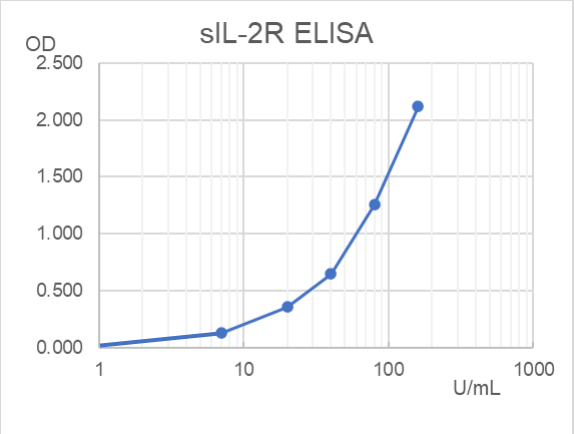
Samples showing concentrations above the measuring range have to be diluted as described in PRE-TEST SETUP INSTRUCTIONS and re-assayed.

In case of diluted samples the values have to be multiplied with the corresponding dilution factor.

**Typical Calibration Curve**

(Example. Do not use for calculation!)

| Standard | sIL-2R | $OD_{mean}$ | $OD/OD_{max}$ |
|---|---|---|---|
| A | 0 U/mL | 0.011 | 1 % |
| B | 7 U/mL | 0.124 | 6 % |
| C | 20 U/mL | 0.354 | 17 % |
| D | 40 U/mL | 0.647 | 31 % |
| E | 80 U/mL | 1.252 | 59 % |
| F | 160 U/mL | 2.116 | 100 % |




**Measuring Range**

The measurement range is defined between the LoQ as functional sensitivity and the upper limit of linearity.

| | |
|---|---|
| Serum | 4.3 - 200 U/mL |
| EDTA plasma | 3.2 - 240 U/mL |
| Heparin plasma | 4.3 - 240 U/mL |
| Citrate plasma | 3.8 - 200 U/mL |

## 16. EXPECTED VALUES

It is recommended that each laboratory establishes its own range of normal values.

The results themselves should not be the only reason for any therapeutic consequences. They have to be correlated to other clinical observations and diagnostic tests.

### 16.1. Reference interval in healthy population

Serum: Reference interval was established in an in-house study testing 173 serum samples of an apparently healthy European population.

Plasma: Reference intervals for human plasma samples were determined by comparison between the different plasma matrices and serum. For this purpose 22 quartet samples (serum, K3-EDTAplasma, Li-heparin plasma, and sodium citrate plasma taken from the same donor) of an apparently healthy European population were tested.

The limits of the expected reference interval are defined as the 2.5$^{th}$ and 97.5$^{th}$ percentile with a confidence interval of 95 %.

Calculated reference intervals for Serum:

| n | Sample matrix | Measured Range | Median | 2.5th - 97.5th Percentile |
|---|---|---|---|---|
| 173 (age: 18 - 71 years) | Serum | 15.7 - 101.3 U/mL | 33.8 U/mL | 19.1 - 68.5 U/mL |

Expected reference intervals for plasma matrices transferred from serum:

| n | Sample matrix | 2.5$^{th}$ - 97.5$^{th}$ Percentile |
|---|---|---|
| 22 | EDTA plasma | 20.2 - 69.6 U/mL |
| 22 | Heparin plasma | 17.8 - 75.2 U/mL |
| 22 | Citrate plasma | 16.4 - 57.9 U/mL |

### 16.2. sIL-2-R levels in affected population

Serum samples from affected population with elevated levels of soluble interleukin-2 receptor showed the following results in in-house measured studies.

| Study | n | Concentration range (min - max) |
|---|---|---|
| 1 | 20 | 90.7 - 314 U/mL |
| 2 | 20 | 82.0 - 490 U/mL |

## 17. LIMITATIONS OF THE PROCEDURE

The following substances do not have a significant effect (+/- 20 % of expected value) on the test results up to the stated concentrations

| | Hemoglobin | Whole blood | Bilirubin | Sodium azide | Biotin | Triglyceride | Albumin |
|---|---|---|---|---|---|---|---|
| **Serum** | ≤ 2 mg/mL | ≤ 1 % | ≤ 1 mg/mL | ≤ 0.5 % | ≤ 3500 ng/mL | ≤ 45 mg/mL | ≤ 25.0 mg/mL |
| **EDTA plasma** | ≤ 2 mg/mL | ≤ 1 % | ≤ 1 mg/mL | ≤ 0.5 % | ≤ 3500 ng/mL | ≤ 45 mg/mL | ≤ 12.5 mg/mL |
| **Heparin plasma** | ≤ 2 mg/mL | ≤ 10 % | ≤ 1 mg/mL | ≤ 0.5 % | ≤ 3500 ng/mL | ≤ 45 mg/mL | ≤ 12.5 mg/mL |
| **Citrate plasma** | ≤ 8 mg/mL | ≤ 1 % | ≤ 1 mg/mL | ≤ 0.5 % | ≤ 3500 ng/mL | ≤ 45 mg/mL | ≤ 12.5 mg/mL |

Specimen collection and storage have a significant effect on the test results. See SPECIMEN COLLECTION AND STORAGE for details. For cross-reactivities, see PERFORMANCE.

## 18. PERFORMANCE

### 18.1. Analytical Specificity (Cross Reactivity)

Due to structural and conformity differences cross reactivity to other human Interleukin receptors is not expected.

### 18.2. Evaluation of Detection Capability

**Limit of Blank (LoB)**

LoB was evaluated based on CLSI guideline EP17-A2. Five blank samples were measured in four replicates per sample over three days with two kit lots.

| | |
|---|---|
| **Limit of Blank** | 1.3 U/mL |

**Limit of Detection (LoD)**

LoD was evaluated based on CLSI guideline EP17-A2. Five different low concentrated samples were measured in four replicates per sample over three days with two reagent lots.

| **Limit of Detection** | |
|---|---|
| Serum | 3.6 U/mL |
| EDTA plasma | 3.2 U/mL |
| Citrate plasma | 4.3 U/mL |
| Heparin plasma | 3.4 U/mL |

**Limit of Quantitation (LoQ) as functional sensitivity**

The LoQ is described as functional sensitivity with a precision goal of 15 %. The study was conducted using five low concentrated samples and three higher concentrated samples, measured in four replicates over three days with two kit lots.

| **Limit of Quantitation** | |
|---|---|
| Serum | 4.3 U/mL |
| EDTA plasma | 3.2 U/mL |
| Citrate plasma | 4.3 U/mL |
| Heparin plasma | 3.8 U/mL |

### 18.3. Linearity

Linearity was evaluated based on CLSI guideline EP06-A. Three different samples, including human serum and plasma (EDTA, citrate, heparin), were diluted with analyte free buffer and the measured values were compared to the predicted values (based on a linear regression).
Linearity is given within ± 20 % of the predicted value.

| **Sample** | **Linear Range** (± 20 % from predicted value) |
|---|---|
| Serum no. 1 | 10.0 - 286 U/mL |
| Serum no. 2 | 10.1 - 197 U/mL |
| Serum no. 3 | 7.2 - 288 U/mL |
| EDTA plasma no. 1 | 8.3 - 289 U/mL |
| EDTA plasma no. 2 | 8.5 - 244 U/mL |
| EDTA plasma no. 3 | 7.8 - 292 U/mL |
| Heparin plasma no. 1 | 8.1 - 201 U/mL |
| Heparin plasma no. 2 | 5.4 - 302 U/mL |
| Heparin plasma no. 3 | 20.6 - 281 U/mL |
| Citrate plasma no. 1 | 12.6 - 289 U/mL |
| Citrate plasma no. 2 | 22.1 - 290 U/mL |
| Citrate plasma no. 3 | 25.4 - 243 U/mL |

### 18.4. Trueness: Calibration / Metrological Traceability

The concentrations assigned are metrological traceable to units / mL by calibration to Non WHO Reference Material NIBSC code 97/600 (Interleukin-2 Soluble Receptor, Human rDNA derived) according to EN ISO 17511:2021.

The combined uncertainty of measurement is calculated as 21.7 % according to the 'Guide to the expression of uncertainty in measurement' (JCGM 100:2008; GUM 1995 with minor corrections).

For soluble interleukin-2-receptor no reference material or internationally recognized standard with assigned concentrations in SI units is available.

The soluble interleukin-2-receptor concentrations assigned to the kit standards and controls of the IBL sInterleukin-2-Receptor ELISA are, therefore, stated in arbitrary units.

Concentrations results from different assays and methods are not displayed in the same units, but the user can apply the Non WHO Reference Material NIBSC code 97/600 with an assigned potency of 1000 units of immunological activity per ampule (is approximately 30 - 100 ng) for comparison and harmonization of results between different assays. It is recommenced that those comparison measurements are performed freshly.

### 18.5. Method comparison versus commercial assay

| Sample | IBL | Commercial assay | n | r |
|---|---|---|---|---|
| Serum/Plasma | sInterleukin-2-Receptor ELISA [U/mL] | IBL 30166211 ELISA [ng/mL] | 50 | 0.983 |
| Serum/Plasma | sInterleukin-2-Receptor ELISA [U/mL] | Commercial assay I [pg/mL] | 63 | 0.907 |
| Serum/Plasma | sInterleukin-2-Receptor ELISA [U/mL] | Commercial assay II [U/mL] | 75 | 0.977 |

### 18.6. Hook effect

Can appear at sandwich assays with a simultaneous incubation of the captor antibody, antigen and detection antibody. To investigate possible high-dose hook effect known high concentrated samples need to be investigated.
The tests are not required because the assay design does not include simultaneous incubation of capture antibody, antigen and detection antibody, therefore a high-dose hook effect is not possible.

### 18.7. Precision

The intra and inter assay precision study was conducted based on CLSI guideline EP05-A3 by testing five different samples (covering the intended matrices, 2 serum samples and 1 sample for each plasma matrix) in duplicate in two runs per day over a period of 20 days using one reagent lot.

| Sample | Mean conc. | Within run (Intra-Assay) | | Between run (Inter-Assay) | |
|---|---|---|---|---|---|
| | | SD | CV | SD | CV |
| 1 | 16.6 U/mL | 0.39 U/mL | 2.4 % | 1.22 U/mL | 7.3 % |
| 2 | 41.5 U/mL | 1.18 U/mL | 2.9 % | 2.71 U/mL | 6.5 % |
| 3 | 55.3 U/mL | 1.57 U/mL | 2.8 % | 3.42 U/mL | 6.2 % |
| 4 | 84.6 U/mL | 2.27 U/mL | 2.7 % | 5.45 U/mL | 6.4 % |
| 5 | 128.9 U/mL | 4.81 U/mL | 3.7 % | 7.9 U/mL | 6.1 % |
| | | | Mean: 2.9 % | | Mean: 6.5 % |

The mean intra assay variation CV is 2.9 % (Range: 2.4 % - 3.7 %) and the mean inter assay variation CV is 6.5 % (Range: 6.1 % - 7.3 %).

The inter lot variation study was conducted during five days of testing. Three kit lots were tested including the kit controls and a panel of five samples (covering the intended matrices, 2 serum samples and 1 sample for each plasma matrix). For each sample five replicates were pipetted.

| Sample | Mean conc. | Total Precision (Inter-Lot) | |
|---|---|---|---|
| | | SD | CV |
| 1 | 13.7 U/mL | 1.81 U/mL | 13.2 % |
| 2 | 23.6 U/mL | 3.23 U/mL | 13.7 % |
| 3 | 49.4 U/mL | 5.18 U/mL | 10.5 % |
| 4 | 83.7 U/mL | 16.43 U/mL | 19.6 % |
| 5 | 114.7 U/mL | 6.82 U/mL | 6.0 % |
| | | | Mean: 12.6 % |

The mean between lot variation CV is 12.6 % (Range: 6.0 % - 19.6 %).

## 19. PRODUCT LITERATURE REFERENCES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# Symbols / Symbole / Symboles / Símbolos / Simboli / Símbolos / Σύμβολα

| | |
|---|---|
| REF | Cat.-No.: / Kat.-Nr.: / No.- Cat.: / Cat.-No.: / N.–Cat.: / N.º Cat.: / Αριθμός-Κατ.: |
| LOT | Lot-No.: / Chargen-Bez.: / No. Lot: / Lot-No.: / Lotto n.: / Lote N.º: / Αριθμός -Παραγωγή: |
| | Use by: / Verwendbar bis: / Utiliser à: / Usado por: / Da utilizzare entro:/ Usar até: / Χρησιμοποιείται από: |
| Σ | No. of Tests: / Kitgröße: / Nb. de Tests: / No. de Determ.: / Quantità dei tests: / N.º de Testes: / Αριθμός εξετάσεων: |
| CONC | Concentrate / Konzentrat / Concentré / Concentrar / Concentrato / Concentrado / Συμπύκνωμα |
| LYO | Lyophilized / Lyophilisat / Lyophilisé / Liofilizado / Liofilizzato / Liofilizado / Λυοφιλιασμένο |
| IVD | In Vitro Diagnostic Medical Device / In-vitro-Diagnostikum / Appareil Médical pour Diagnostics In Vitro / Dispositivo Médico para Diagnóstico In Vitro / Dispositivo Medico Diagnostico In vitro / Equipamento Médico de Diagnóstico In Vitro / Ιατρική συσκευή για In-Vitro Διάγνωση |
| BIO | Contains biological material of human origin / Enthält biologisches Material menschlichen Ursprungs / Contient une substance biologique d'origine humaine / Contiene material biológico de origen humano / Contiene materiale biologico di origine umana / Contém material biológico de origem humana / Περιέχει βιολογικό υλικό ανθρώπινης προέλευσης |
| BIO | Contains biological material of animal origin / Enthält biologisches Material tierischen Ursprungs / Contient une substance biologique d'origine animale / Contiene material biológico de origen animal / Contiene materiale biologico di origine animale / Contém material biológico de origem animal / Περιέχει βιολογικό υλικό ζωικής προέλευσης |
| UDI | Unique Device Identification / Eindeutige Gerätekennung / Identifiant de dispositif unique / Identificación única de producto / Identificatore univoco del dispositivo / Identificador de dispositivo único / Μοναδικός αναγνωριστικός κωδικός προϊόντος |
| | Read instructions before use / Arbeitsanleitung lesen / Lire la fiche technique avant emploi / Lea las instrucciones antes de usar / Leggere le istruzioni prima dell'uso / Ler as instruções antes de usar / Διαβάστε τις οδηγίες πριν την χρήση |
| | Keep away from heat or direct sun light / Vor Hitze und direkter Sonneneinstrahlung schützen / Garder à l'abri de la chaleur et de toute exposition lumineuse / Manténgase alejado del calor o la luz solar directa / Non esporre ai raggi solari / Manter longe do calor ou luz solar directa / Να φυλάσσεται μακριά από θερμότητα και άμεση επαφή με το φως του ηλίου |
| | Store at: / Lagern bei: / Stocker à: / Almacene a: / Armazenar a: / Conservare a: / Armazenar em: / Αποθήκευση στους: |
| 2-8°C | Store at: 2 - 8°C / Lagern bei: 2 - 8°C / Stocker à: 2 - 8°C / Almacene a: 2 - 8°C / Armazenar a: 2 - 8°C / Conservare a: 2-8°C / Armazenar em: 2-8°C / Αποθήκευση στους: 2-8°C |
| | Manufacturer: / Hersteller: / Fabricant: / Productor: / Fabricante: / Fabbricante: / Παραγωγός: |
| | Distributor: / Distributor: / Distributeur: / Distributor: / Distributore: / Distribuidor: / Διανομέας: |
| | Caution! / Vorsicht! / Attention! / ¡Precaución! / Attenzione! / Cuidado! / Προσοχή! |
| | Symbols of the kit components see MATERIALS SUPPLIED.<br>Die Symbole der Komponenten sind im Kapitel KOMPONENTEN DES KITS beschrieben.<br>Voir MATERIEL FOURNI pour les symbôles des composants du kit.<br>Símbolos de los componentes del juego de reactivos, vea MATERIALES SUMINISTRADOS.<br>Per i simboli dei componenti del kit si veda COMPONENTI DEL KIT.<br>Para símbolos dos componentes do kit ver MATERIAIS FORNECIDOS.<br>Για τα σύμβολα των συστατικών του κιτ συμβουλευτείτε το ΠΑΡΕΧΟΜΕΝΑ ΥΛΙΚΑ. |

Generic table, not all symbols are present in the product

COMPLAINTS: Complaints may be submitted initially written or vocal. Subsequently they need to be filed including the test performance and results in writing in case of analytical reasons.

WARRANTY: The product is warranted to be free from material defects within the specific shelf life and to comply with product specifications delivered with the product. The product must be used according to the Intended use, all instructions given in the instructions for use and within the product specific shelf life. Any modification of the test procedure or exchange or mixing of components of different lots could negatively affect the results. These cases invalidate any claim for replacement.

LIMITATION OF LIABILITY: IN ALL CIRCUMSTANCES THE EXTENT OF MANUFACTURER'S LIABILITY IS LIMITED TO THE PURCHASE PRICE OF THE KIT(S) IN QUESTION. IN NO EVENT SHALL MANUFACTURER BE LIABLE FOR ANY INCIDENTAL OR CONSEQUENTIAL DAMAGES, INCLUDING DAMAGES FOR LOST PROFITS, LOST SALES, INJURY TO PERSON OR PROPERTY OR ANY OTHER INCIDENTAL OR CONSEQUENTIAL LOSS.

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For further country-specific classifications, please refer to the corresponding safety data sheet.

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