Elecsys Interferon Gamma

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REF		Σ	SYSTEM
09437622190	09437622500	300	**cobas e** 402 **cobas e** 801

English

System information

Short name	ACN (application code number)
IFN G	10245

Intended use

Elecsys Interferon Gamma is an immunoassay for the in vitro quantitative determination of interferon gamma level in human plasma samples. It is intended as an aid in the identification of patients with elevated level of interferon gamma indicating an inflammatory state or a sensitized immune system.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

Summary

Interferons (IFNs) were initially described as agents interfering with viral multiplication and eliciting potent anti-viral activity[1], and include 3 currently recognized families – type I, II and III IFNs.[1] The cytokine interferon gamma (IFN-γ) is the sole member of the type II interferon family discovered almost 60 years ago[1,2], and has been shown to exhibit a vast array of physiological functions, including cytostatic, pro-apoptotic and anti-proliferative functions.[2]

IFN-γ is a pleiotropic cytokine and plays an important role in coordinating both innate and adaptive immune responses.[2] It has been shown to exert a myriad of effects on both host defense and immune regulation, including antiviral, antimicrobial, antitumor activities[3,4], autoimmune diseases[5], diverse types of chronic inflammatory conditions[6,7,3,8,9], and several neurodegenerative diseases.[7,10,11,12,13]

IFN-γ is produced by selected cell types of the innate and adaptive immune system, including macrophages, dendritic cells, natural killer (NK) cells, NKT cells, ILC1 (cytokine-activated group 1 innate lymphoid cells), neutrophils, B and T cells.[2,7,14,15] It exerts its biological function by binding to the IFN-γ receptor, which is present on immune as well as tissue cell types. Upon activation, IFN-γ receptor initiates a cascade of intracellular signaling events leading to transcriptional regulation of the target genes.[7,3] Functionally, IFN-γ induces T cell activation and T helper cell 1 (Th1) polarization[4], functions as the primary activator of macrophages, and stimulates NK cells and neutrophils.[16] This complex interplay between immune cell activities and IFN-γ leads to the initiation of a cascade of pro-inflammatory responses.[7] While IFN-γ generates a self-amplifying positive feedback loop, which has been detected in both tumor and inflamed environments[2], it can also prevent over-activation of the immune system and tissue damage by orchestrating numerous protective functions in infections and cancer.[7] This balance is maintained by complex mechanisms, which are not yet fully understood.[2]

IFN-γ has been explored as a biomarker associated with various infectious diseases. Elevated serum or plasma IFN-γ levels have been reported in patients suffering various infections including severe fever with thrombocytopenia syndrome virus (SFTSV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), hepatitis B virus, influenza virus A/B, latent tuberculosis infection, Salmonella typhimurium, Burkholderia pseudomallei, Salmonella and Chlamydia trachomatis.[7,17,18,19,20,21,22,23,24] Additionally, elevated IFN-γ levels have been reported in inflammatory, neurodegenerative and autoimmune conditions such as preeclampsia[25,26], inflammatory bowel disease[27], atherosclerosis and chronic heart failure[7,28,29], amyotrophic lateral sclerosis (ALS)[7,30], Alzheimer's disease[31], Parkinson's disease[7,9], and multiple sclerosis (MS).[13] Furthermore, IFN-γ detection is an integral component of IFN-γ release assays (IGRA) where IFN-γ release is used as a reporter for T cell activation upon in vitro stimulation. IGRA assays have been established as an aid in diagnosis of latent Mycobacterium tuberculosis infections[32,33], and are currently being explored for the detection of anti-SARS-CoV-2 T cell response.[34]

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 18 µL of sample are incubated with monoclonal antibodies specific against human IFN-γ labeled with a ruthenium complex[a)].
- 2nd incubation: After addition of streptavidin-coated microparticles and a biotinylated monoclonal antibody specific against human IFN-γ, a sandwich-complex is formed between the antibodies and the analyte, which then becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell II M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the **cobas** link.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$)

Reagents - working solutions

The **cobas e** pack is labeled as IFN G.

M Streptavidin-coated microparticles, 1 bottle, 12.4 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Anti-hIFN-γ~$Ru(bpy)_3^{2+}$, 1 bottle, 18.8 mL:
Ruthenylated monoclonal antibodies against human IFN-γ < 2.5 µg/mL, pH 5.8; preservative.

R2 Anti-hIFN-γ~biotin, 1 bottle, 18.8 mL:
Biotinylated monoclonal antibody against human IFN-γ ≤ 1 µg/mL, pH 5.8; preservative.

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317	May cause an allergic skin reaction.
Prevention:	
P261	Avoid breathing mist or vapours.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves.
Response:	
P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.

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Disposal:

P501 Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Reagent handling

For professional use.

The reagents in the kit have been assembled into a ready-for-use unit that cannot be separated.

All information required for correct operation is available via the **cobas** link.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the **cobas e** pack **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability:	
unopened at 2-8 °C	up to the stated expiration date
on the analyzers	16 weeks

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

Li-heparin, Na-heparin, K_2-EDTA, K_3-EDTA and CPDA plasma.

Plasma tubes containing separating gel can be used.

Criterion: Slope 1.00 ± 0.10 + intercept ≤ 0.10 IU/mL.

For native samples collected in sodium citrated plasma: Slope 0.84 ± 0.10.

Sampling devices containing liquid anticoagulants have a dilution effect resulting in lower values (IU/mL) for individual patient specimens. In order to minimize dilution effects it is essential that respective sampling devices are filled completely according to manufacturer's instruction. For citrated plasma (1 part citrate solution + 9 parts blood), the dilution effect must be taken into account.

Stable for 7 days at 15-25 °C, 7 days at 2-8 °C, 3 months at -20 °C (± 5 °C). Freeze only once.

The sample types listed were tested with a selection of sample collection tubes or systems that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube/collection system manufacturer.

Specimens should not be subsequently altered with additives (e.g. biocides, anti-oxidants or substances that could possibly change the pH or ionic strength of the sample) in order to avoid erroneous findings.

Centrifuge samples containing precipitates and thawed samples before performing the assay.

Do not use heat-inactivated samples.

Do not use samples and controls stabilized with azide.

Ensure the samples and calibrators are at 20-25 °C prior to measurement.

Due to possible evaporation effects, samples and calibrators on the analyzers should be analyzed/measured within 2 hours.

The performance of the Elecsys Interferon Gamma assay has not been established with cadaveric samples.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- REF 09437657190, CalSet Interferon Gamma, 4 x 1.0 mL
- REF 09437665190, PreciControl Interferon Gamma, 4 x 1.0 mL
- REF 07299001190, Diluent Universal, 36 mL sample diluent
- General laboratory equipment
- **cobas e** analyzer

Additional materials for **cobas e** 402 and **cobas e** 801 analyzers:

- REF 06908799190, ProCell II M, 2 x 2 L system solution
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 07485409001, Reservoir Cup, 8 cups to supply ProCell II M and CleanCell M
- REF 06908853190, PreClean II M, 2 x 2 L wash solution
- REF 05694302001, Assay Tip/Assay Cup tray, 6 magazines x 6 magazine stacks x 105 assay tips and 105 assay cups, 3 wasteliners
- REF 07485425001, Liquid Flow Cleaning Cup, 2 adaptor cups to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning Detection Unit
- REF 07485433001, PreWash Liquid Flow Cleaning Cup, 1 adaptor cup to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning PreWash Unit
- REF 11298500316, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

Resuspension of the microparticles takes place automatically prior to use.

Place the cooled (stored at 2-8 °C) **cobas e** pack on the reagent manager. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the **cobas e** pack.

Calibration

Traceability: The Elecsys Interferon Gamma assay has been standardized against the first British INTERFERON GAMMA (HUMAN, LEUKOCYTE-DERIVED) standard, NIBSC code: 82/587.

Every Elecsys reagent set has a barcoded label containing specific information for calibration of the particular reagent lot. The predefined master curve is adapted to the analyzer using the relevant CalSet.

Calibration frequency: Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the **cobas e** pack was registered on the analyzer).

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Renewed calibration is recommended as follows:

- after 12 weeks when using the same reagent lot
- after 7 days when using the same **cobas e** pack on the analyzer
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PreciControl Interferon Gamma.

In addition, other suitable control material can be used.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per **cobas e** pack, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

If necessary, repeat the measurement of the samples concerned.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

The analyzer automatically calculates the analyte concentration of each sample in IU/mL or pg/mL (selectable).

Conversion factor: IU/mL x 50 = pg/mL

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Limitations - interference

The effect of the following endogenous substances and pharmaceutical compounds on assay performance was tested. Interferences were tested up to the listed concentrations and no impact on results was observed.

Endogenous substances

Compound	Concentration tested
Bilirubin	≤ 1129 µmol/L or ≤ 66 mg/dL
Hemoglobin	≤ 1000 mg/dL or ≤ 10 g/L
Intralipid	≤ 2000 mg/dL
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Rheumatoid factors	≤ 1200 IU/mL
IgG	≤ 5.0 g/dL or ≤ 50 g/L
IgA	≤ 1.6 g/dL or ≤ 16 g/L
IgM	≤ 1.0 g/dL or ≤ 10 g/L

Criterion: For concentrations of 0.07-1.0 IU/mL the deviation is ≤ 0.15 IU/mL. For concentrations > 1.0 IU/mL the deviation is ≤ 15 %.

Peak concentrations upon intravenous immunoglobulin (IVIG) treatment may interfere with the Elecsys Interferon Gamma assay.

No false low results due to a high-dose hook effect were found up to 2500 IU/mL with the Elecsys Interferon Gamma assay but occurrence of high-dose hook effect cannot be completely excluded.

Pharmaceutical substances
In vitro tests were performed on 17 commonly used pharmaceuticals. No interference with the assay was found.

In addition, 22 pharmaceuticals were tested. No interference with the assay was found.

Drug interferences are measured based on recommendations given in CLSI guidelines EP07 and EP37 and other published literature. Effects of concentrations exceeding these recommendations have not been characterized.

In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

Limits and ranges

Measuring range

0.07-160 IU/mL (defined by the Limit of Detection and the maximum of the master curve). Values below the Limit of Detection are reported as < 0.07 IU/mL. Values above the measuring range are reported as > 160 IU/mL.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank = 0.03 IU/mL

Limit of Detection = 0.07 IU/mL

Limit of Quantitation = 0.1 IU/mL

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples. The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is defined as the lowest amount of analyte in a sample that can be accurately quantified with a total error ≤ 30 %. It has been determined using samples with low concentration of spiked human interferon gamma.

Dilution

Samples with interferon gamma concentrations above the measuring range can be diluted with Diluent Universal. The recommended dilution factor is 1:5 (automatically by the analyzers). The concentration of the diluted sample must be ≥ 30 IU/mL.

After dilution by the analyzers, the software automatically takes the dilution into account when calculating the sample concentration.

Expected values

In a study the Elecsys Interferon Gamma assay was used on samples from 436 apparently healthy individuals. With these 436 data points, a threshold value of 0.099 IU/mL was determined. This value respresents the 97.5th percentile.

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using Elecsys reagents, samples and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84). The following results were obtained:

cobas e 402 and **cobas e** 801 analyzers					
		Repeatability		**Intermediate precision**	
Sample	Mean IU/mL	SD IU/mL	CV %	SD IU/mL	CV %
Human plasma 1	0.468	0.00523	1.1	0.00808	1.7
Human plasma 2	3.12	0.0303	1.0	0.0502	1.6
Human plasma 3	16.6	0.158	1.0	0.257	1.5
Human plasma 4	65.1	0.919	1.4	1.13	1.7
Human plasma 5	88.7	0.819	0.9	1.22	1.4
PC IFNG[b)]1	0.899	0.0121	1.3	0.0170	1.9
PC IFNG2	14.7	0.214	1.5	0.259	1.8

b) PC IFNG = PreciControl Interferon Gamma

Method comparison

a) A comparison of the Elecsys Interferon Gamma assay, REF 09437622190, (**cobas e** 801 analyzer; x), with the Elecsys Interferon Gamma assay REF 09437622190 (**cobas e** 402 analyzer; y), gave the following correlations (IU/mL):

Number of samples measured: 122

Passing/Bablok[35]

y = 1.055x - 0.0240

τ = 0.997

The sample concentrations were between 0.133 and 149 IU/mL.

b) A comparison of the Elecsys Interferon Gamma assay, REF 09437622190, (**cobas e** 801 analyzer; x), with the Elecsys Interferon Gamma assay REF 09437568190 (**cobas e** 601 analyzer; y), gave the following correlations (IU/mL):

Number of samples measured: 122

Passing/Bablok[35]

y = 1.016x - 0.044

τ = 1.000

The sample concentrations were between 0.133 and 149 IU/mL.

Analytical specificity

Potential cross-reactivity of the Elecsys Interferon Gamma assay was tested using plasma containing human interferon gamma in 2 concentration

ranges, which had been spiked with potentially cross-reacting substances up to 50 ng/mL.

The Elecsys Interferon Gamma assay did not show any significant cross-reactivity with the following substances, tested with IFN-γ concentrations of approximately 5 IU/mL and approximately 20 IU/mL:
Interferon-alpha, Interferon-beta, Interferon-lambda, Interleukin-1alpha, Interleukin-1beta, Interleukin-2, Interleukin-3, Interleukin-4, Interleukin-5, Interleukin-6, Interleukin-8, Interleukin-10, Interleukin-12, Interleukin-13, Interleukin-17, tumor necrosis factor-alpha.

The Elecsys Interferon Gamma assay is designed to detect and quantify human interferon gamma; interferon gamma from other species was not assessed and a cross-reactivity cannot be ruled out.

References

1 Schroder K, Hertzog PJ, Ravasi T, et al. Interferon-γ: An Overview of Signals, Mechanisms and Functions. J Leukoc Biol 2004 Feb;75(2):163-189.

2 Jorgovanovic D, Song M, Wang L, et al. Roles of IFN-γ in Tumor Progression and Regression: A Review. Biomark Res 2020;8:49.

3 Voloshyna I, Littlefield MJ, Reiss AB. Atherosclerosis and Interferon-Gamma: New Insights and Therapeutic Targets. Trends Cardiovasc Med 2014 Jan;24(1):45-51.

4 Zhu X, Zhu J. Cd4 T Helper Cell Subsets and Related Human Immunological Disorders. Int J Mol Sci 2020 Oct 28;21(21).

5 Shin MS, Lee N, Kang I. Effector T-Cell Subsets in Systemic Lupus Erythematosus: Update Focusing on Th17 Cells. Curr Opin Rheumatol 2011 Sep;23(5):444-448.

6 Moss JW, Ramji DP. Interferon-Gamma: Promising Therapeutic Target in Atherosclerosis. World J Exp Med 2015 Aug 20;5(3):154-159.

7 Kak G, Raza M, Tiwari BK. Interferon-Gamma (IFN-γ): Exploring Its Implications in Infectious Diseases. Biomol Concepts 2018 May 30;9(1):64-79.

8 Verstappen GM, Corneth OBJ, Bootsma H, et al. Th17 Cells in Primary Sjogren's Syndrome: Pathogenicity and Plasticity. J Autoimmun 2018 Feb;87:16-25.

9 Kato M. New Insights into IFN-γ in Rheumatoid Arthritis: Role in the Era of Jak Inhibitors. Immunol Med 2020 Jun;43(2):72-78.

10 Mount MP, Lira A, Grimes D, et al. Involvement of Interferon-Gamma in Microglial-Mediated Loss of Dopaminergic Neurons. J Neurosci 2007 Mar 21;27(12):3328-3337.

11 Saghazadeh A, Ataeinia B, Keynejad K, et al. A Meta-Analysis of Pro-Inflammatory Cytokines in Autism Spectrum Disorders: Effects of Age, Gender, and Latitude. J Psychiatr Res 2019 Aug;115:90-102.

12 Yahyapour R, Amini P, Rezapour S, et al. Radiation-Induced Inflammation and Autoimmune Diseases. Mil Med Res 2018 Mar 20;5(1):9.

13 Danikowski KM, Jayaraman S, Prabhakar BS. Regulatory T Cells in Multiple Sclerosis and Myasthenia Gravis. J Neuroinflammation 2017 Jun 9;14(1):117.

14 Fuchs A, Vermi W, Lee JS, et al. Intraepithelial Type 1 Innate Lymphoid Cells Are a Unique Subset of IL-12- and IL-15-Responsive IFN-γ-Producing Cells. Immunity 2013 Apr 18;38(4):769-781.

15 Mezouar S, Mege JL. Changing the Paradigm of IFN-γ at the Interface between Innate and Adaptive Immunity: Macrophage-Derived IFN-γ. J Leukoc Biol 2020 Jul;108(1):419-426.

16 Sikorski K, Czerwoniec A, Bujnicki JM, et al. STAT1 as a Novel Therapeutical Target in Pro-Atherogenic Signal Integration of IFNγ, TLR4 and IL-6 in Vascular Disease. Cytokine Growth Factor Rev 2011 Aug;22(4):211-219.

17 Lauw FN, Simpson AJ, Prins JM, et al. Elevated Plasma Concentrations of Interferon (IFN)-Gamma and the IFN-Gamma-Inducing Cytokines Interleukin (IL)-18, IL-12, and IL-15 in Severe Melioidosis. J Infect Dis 1999 Dec;180(6):1878-1885.

18 Ning YJ, Mo Q, Feng K, et al. Interferon-γ-Directed Inhibition of a Novel High-Pathogenic Phlebovirus and Viral Antagonism of the Antiviral Signaling by Targeting STAT1. Front Immunol 2019;10:1182.

19 Chu CM, Sheen IS, Yeh CT, et al. Serum Levels of Interferon-Alpha and -Gamma in Acute and Chronic Hepatitis B Virus Infection. Dig Dis Sci 1995 Oct;40(10):2107-2112.

20 Sato M, Hosoya M, Wright PF. Differences in Serum Cytokine Levels between Influenza Virus a and B Infections in Children. Cytokine 2009 Jul;47(1):65-68.

21 Ziklo N, Huston WM, Taing K, et al. High Expression of IDO1 and TGF-β1 During Recurrence and Post Infection Clearance with Chlamydia Trachomatis, Are Independent of Host IFN-γ Response. BMC Infect Dis 2019 Mar 4;19(1):218.

22 Huaman MA, Deepe GS, Jr., Fichtenbaum CJ. Elevated Circulating Concentrations of Interferon-Gamma in Latent Tuberculosis Infection. Pathog Immun 2016 Fall-Winter;1(2):291-303.

23 Califano D, Furuya Y, Roberts S, et al. IFN-γ Increases Susceptibility to Influenza a Infection through Suppression of Group II Innate Lymphoid Cells. Mucosal Immunol 2018 Jan;11(1):209-219.

24 Yarmohammadi A, Yarmohammadi M, Fakhri S, et al. Targeting Pivotal Inflammatory Pathways in Covid-19: A Mechanistic Review. Eur J Pharmacol 2021 Jan 5;890:173620.

25 Deng Z, Zhang L, Tang Q, et al. Circulating Levels of IFN-γ, IL-1, IL-17 and IL-22 in Pre-Eclampsia: A Systematic Review and Meta-Analysis. Eur J Obstet Gynecol Reprod Biol 2020 May;248:211-221.

26 Yang Y, Su X, Xu W, et al. Interleukin-18 and Interferon Gamma Levels in Preeclampsia: A Systematic Review and Meta-Analysis. Am J Reprod Immunol 2014 Nov;72(5):504-514.

27 Roberts-Thomson IC, Fon J, Uylaki W, et al. Cells, Cytokines and Inflammatory Bowel Disease: A Clinical Perspective. Expert Rev Gastroenterol Hepatol 2011 Dec;5(6):703-716.

28 Mangge H, Stelzer I, Reininghaus EZ, et al. Disturbed Tryptophan Metabolism in Cardiovascular Disease. Curr Med Chem 2014 Jun;21(17):1931-1937.

29 Cheng X, Ding Y, Xia C, et al. Atorvastatin Modulates Th1/Th2 Response in Patients with Chronic Heart Failure. J Card Fail 2009 Mar;15(2):158-162.

30 Liu J, Gao L, Zang D. Elevated Levels of IFN-γ in CSF and Serum of Patients with Amyotrophic Lateral Sclerosis. PLoS One 2015;10(9):e0136937.

31 Niranjan R. Molecular Basis of Etiological Implications in Alzheimer's Disease: Focus on Neuroinflammation. Mol Neurobiol 2013 Dec;48(3):412-428.

32 Campbell JR, Winters N, Menzies D. Absolute Risk of Tuberculosis among Untreated Populations with a Positive Tuberculin Skin Test or interferon-Gamma Release Assay Result: Systematic Review and Meta-Analysis. BMJ 2020 Mar 10;368:m549.

33 Zhou Q, Chen YQ, Qin SM, et al. Diagnostic Accuracy of T-Cell Interferon-γ Release Assays in Tuberculous Pleurisy: A Meta-Analysis. Respirology 2011 Apr;16(3):473-480.

34 Murugesan K, Jagannathan P, Pham TD, et al. Interferon-γ Release Assay for Accurate Detection of Severe Acute Respiratory Syndrome Coronavirus 2 T-Cell Response. Clin Infect Dis 2021 Nov 2;73(9):e3130-e3132.

35 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets and the Method Sheets of all necessary components (if available in your country).

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Any serious incident that has 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.

The Summary of Safety & Performance Report can be found here: https://ec.europa.eu/tools/eudamed

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Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.roche.com for definition of symbols used):

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
CALIBRATOR	Calibrator
→	Volume for reconstitution
GTIN	Global Trade Item Number

CE 0123

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