Elecsys AFP

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REF		Σ	SYSTEM
09015124190	09015124500	300	**cobas e** 402 **cobas e** 801

English

System information

Short name	ACN (application code number)
AFP	10209

Please note

The measured AFP value of a patient's sample can vary depending on the testing procedure used. The laboratory finding must therefore always contain a statement on the AFP assay method used. AFP values determined on patient samples by different testing procedures cannot be directly compared with one another and could be the cause of erroneous medical interpretations.

If there is a change in the AFP assay procedure used while monitoring therapy, then the AFP values obtained upon changing over to the new procedure must be confirmed by parallel measurements with both methods.

Intended use

Immunoassay for the in vitro quantitative determination of α_1-fetoprotein in human serum and plasma.

This assay is intended for the use as:

- An aid in the diagnosis of hepatocellular carcinoma (HCC).
- An aid in the management of patients with non-seminomatous germ cell tumors.
- One component in combination with other parameters to evaluate the risk of trisomy 21 (Down syndrome). Further testing is required for diagnosis of chromosomal aberrations.

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

Summary

Alpha1-fetoprotein (AFP), an albumin-like glycoprotein with a molecular weight of approximately 70 kDa, is formed in the yolk sac during fetal life, in non-differentiated liver cells, and the fetal gastro-intestinal tract.[1,2]

Tumors that synthesize AFP are mainly testicular non-seminomatous germ cell tumors (NSGCT), yolk sac tumors of the ovary and hepatocellular carcinoma (HCC). Moreover AFP is an important part in the risk assessment for trisomy 21 in the second trimester of pregnancy together with hCG+β and other parameters.[3]

Testicular cancer

Careful monitoring of the serum tumor markers AFP and human chorionic gonadotropin (hCG) is essential in the management of patients with germ cell tumors (GCT), as these markers are important for diagnosis, as prognostic indicators, in monitoring treatment response, and in the detection of early relapse.[4] In addition, hCG and AFP are important parameters for estimating the survival rate of patients with advanced NSGCTs and are also recommended by the National Academy of Clinical Biochemistry for the management of such patients.[5]

Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is frequently the result of advanced liver disease and can develop in patients with and without cirrhosis.[6] AFP has long been recognized as a biomarker for HCC, and has played a prominent role in the diagnosis of HCC. Substantially elevated AFP values can indicate primary liver cell carcinoma and it has been shown that AFP levels increase with tumor size.[7] Diagnosis of HCC has primarily relied on the presence of typical features seen on contrast-enhanced imaging studies, histopathological assessment, and serum AFP levels.[8] While AFP is elevated during hepato-carcinogenesis, it can also be found in other tumors such as testicular, embryonic or gastric cancer.[9,10] AFP has reported sensitivities ranging from 39 to 65 %, and specificities from 76 to 94 % in HCC patients.[11] The divergence in sensitivity and specificity of AFP in these studies is probably due to a variety of factors including different etiologies, variable study designs, and different cutoff values. As the AFP values can also rise during regeneration of the liver, moderately elevated values are found in alcohol-mediated liver cirrhosis and acute viral hepatitis.[12] Surveillance of patients at risk for developing HCC by abdominal ultrasonography in combination with AFP is recommended by several clinical practice guidelines.[13,14,15]

Trisomy 21

Measurement of AFP makes a contribution to the risk assessment for trisomy 21 (Down syndrome) in the second trimester of pregnancy together with hCG+β and other parameters, such as exact gestational age and maternal weight.[3] In a trisomy 21 affected pregnancy the maternal serum concentration of AFP is decreased whereas the maternal serum hCG+β concentration is approximately twice the normal median.[16] The risk for a trisomy 21 affected pregnancy in the second trimester can be calculated by a suitable software (see "Materials required, but not provided" section) using the algorithm as described by Cuckle et al.[17] and the respective assay specific parameters.[18,19,20,21,22]

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 6 µL of sample, a biotinylated monoclonal AFP-specific antibody, and a monoclonal AFP-specific antibody labeled with a ruthenium complex[a)] react to form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex 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 AFP.

M Streptavidin-coated microparticles, 1 bottle, 14.1 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Anti-AFP-Ab~biotin, 1 bottle, 19.7 mL:
Biotinylated monoclonal anti-AFP antibodies (mouse) 4.5 mg/L; phosphate buffer 100 mmol/L, pH 6.0; preservative.

R2 Anti-AFP-Ab~$Ru(bpy)_3^{2+}$, 1 bottle, 19.7 mL:
Monoclonal anti-AFP antibodies (mouse) labeled with ruthenium complex 12.0 mg/L; phosphate buffer 100 mmol/L, pH 6.0; 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:

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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.

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

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.

Serum collected using standard sampling tubes or tubes containing separating gel.

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

Plasma tubes containing separating gel can be used.

Criterion: Slope 0.9-1.1 + coefficient of correlation ≥ 0.95.

Stable for 5 days at 20-25 °C, 14 days at 2-8 °C, 6 months at -20 °C (± 5 °C). The samples may be frozen 3 times.

The suitability of plasma samples for estimating the risk of trisomy 21 has not been evaluated.

The sample types listed were tested with a selection of sample collection tubes 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 manufacturer.

Centrifuge samples containing precipitates 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.

Materials provided

See “Reagents – working solutions” section for reagents.

Materials required (but not provided)

- REF 09227261190, AFP CalSet II, for 4 x 1.0 mL
- REF 11776452122, PreciControl Tumor Marker, for 4 x 3.0 mL or
  REF 11731416190, PreciControl Universal, for 4 x 3.0 mL or
  REF 08754551190, PreciControl HCC V2, for 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

For risk calculation of trisomy 21:

- A suitable software, e.g.
  REF 05126193, SsdwLab (V5.0 or later), single user licence
  REF 05195047, SsdwLab (V5.0 or later), multi user licence
- REF 03271749190, HCG+β, 100 tests
- REF 07251025190, Elecsys HCG+β, 300 tests
- REF 03302652190, HCG+β CalSet, for 4 x 1.0 mL

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: This method has been standardized against the 1st IRP WHO Reference Standard 72/225.

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 28 days when using the same **cobas e** pack on the analyzer
- as required: e.g. quality control findings outside the defined limits

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Quality control

For quality control, use PreciControl Tumor Marker or PreciControl Universal or PreciControl HCC V2.

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 either in IU/mL, ng/mL, kIU/L or additionally in IU/L.

Conversion factors: IU/mL x 1.21 = ng/mL

ng/mL x 0.83 = IU/mL

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	≤ 1112 µmol/L or ≤ 65 mg/dL
Hemoglobin	≤ 1.37 mmol/L or ≤ 2200 mg/dL
Intralipid	≤ 1500 mg/dL
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Rheumatoid factors	≤ 1500 IU/mL

Criterion: Recovery of ± 0.4 IU/mL of initial value for samples ≤ 4 IU/mL, within ± 10 % of initial value for samples > 4 IU/mL.

There is no high-dose hook effect at AFP concentrations up to 1 million IU/mL (1.21 million ng/mL).

Pharmaceutical substances

In vitro tests were performed on 16 commonly used pharmaceuticals. No interference with the assay was found.

In addition, the following special cancer drugs were tested. No interference with the assay was found.

Special cancer drugs

Drug	Concentration tested (mg/L)
Doxorubicin	75
Cyclophosphamide	1000
Cisplatin	225
5-Fluorouracil	500
Methotrexate	1000
Tamoxifen	50
Mitomycin	25
Carboplatin	1000
Etoposide	400
Taxol	5.5

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

0.75-1000 IU/mL or 0.908-1210 ng/mL (defined by the Limit of Blank and the maximum of the master curve). Values below the Limit of Blank are reported as < 0.75 IU/mL or < 0.908 ng/mL. Values above the measuring range are reported as > 1000 IU/mL or > 1210 ng/mL (or up to 50000 IU/mL or 60500 ng/mL for 50-fold diluted samples).

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank = 0.75 IU/mL (or 0.91 ng/mL)

Limit of Detection = 1.5 IU/mL (or 1.82 ng/mL)

Limit of Quantitation = 2.25 IU/mL (or 2.72 ng/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 the lowest analyte concentration that can be reproducibly measured with an intermediate precision CV of ≤ 20 %.

Dilution

Samples with AFP concentrations above the measuring range can be diluted with Diluent Universal. The recommended dilution is 1:50 (either automatically by the analyzers or manually). The concentration of the diluted sample must be > 18 IU/mL (> 21.8 ng/mL).

After manual dilution, multiply the result by the dilution factor.

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

Expected values

Results of following studies using the Elecsys AFP assay see below:

a) Multicenter study "Elecsys 2010 analyzer" status September 1997 and reference range study in Germany and France, data evaluated in September 1998.

Following AFP values were found in serum samples from 646 healthy test subjects:

≤ 5.8 IU/mL or ≤ 7.0 ng/mL for 95 % of the results.

AFP median values for completed weeks of pregnancy (defined as completed weeks of pregnancy beginning with the start of the last menstruation phase):

Weeks	14	15	16	17	18	19
N	382	1782	2386	975	353	146
IU/mL	23.2	25.6	30.0	33.5	40.1	45.5
ng/mL	27.9	30.9	36.1	40.4	48.3	54.8

b) Multicenter study to determine reference values for evaluating the risk of trisomy 21 in maternal serum (study No. BO1P019).

Values from serum samples of 1753 pregnant women in total (relevant gestational weeks 14 to 18) were evaluated.

Measurements with the Elecsys HCG+β assay and the Elecsys AFP assay were conducted in 5 clinical centers in Belgium, France, and Germany.

The gestational age in days determined by ultrasound was given for each sample. From a log-linear regression analysis of all 1753 AFP values versus gestational age the following median values were calculated for the middle of the respective weeks (e.g. week 14 + 3 days):

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Weeks	14	15	16	17	18
IU/mL	20.9	24.0	27.6	31.7	36.4
ng/mL	25.3	29.0	33.3	38.3	44.0

Note: For prenatal testing it is recommended that the median values be re-evaluated periodically (1 to 3 years) and whenever methodology changes.

The transferability of the reference values to plasma samples has not been verified.

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

Elecsys AFP as an aid in the diagnosis of HCC

A prospective multicenter study (Roche study No. RD002542 and RD002543) to evaluate the clinical performance of Elecsys AFP as an aid in the diagnosis of HCC included 376 patients with liver disease, of which 168 had HCC and 208 had liver disease but no diagnosis of HCC (control).

	Median age	Gender (% male)	Race				
			Asian (%)	Caucasian (%)	Black (%)	Other (%)	Missing (%)
Control	53	60.6	47.6	48.6	1.4	0	2.4
HCC	64	83.9	42.3	56.5	0	0.6	0.6

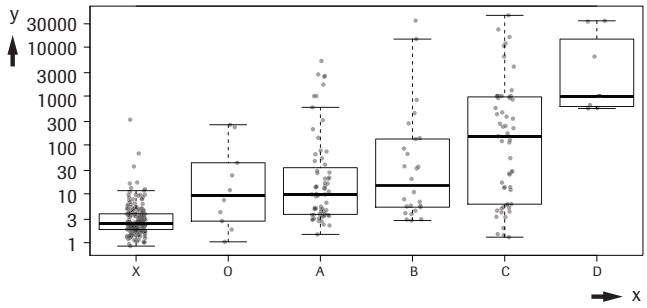
a) **Range of AFP concentration in HCC cases compared to controls**

The following table and graph show the range of AFP concentration in samples from HCC patients staged according to Barcelona clinic liver cancer classification (BCLC)[23] compared to controls. For the 168 patients with a diagnosis of HCC, the AFP concentration increased with disease progression, especially in late stage disease. All concentrations in the table are in IU/mL and (ng/mL), while concentrations in the graph are in IU/mL. The thick line in the box plots represents the median value.

Disease stage	N	Min/Max	Mean ± SD	Median	25th-75th perc. b)
Control c)	208	0.85/327.84 (1.03/396.69)	5.33±23.15 (6.45±28.01)	2.42 (2.92)	1.86-3.89 (2.25-4.71)
Early (Stage 0 + A)	77	1.04/5224 (1.26/6322)	252±799 (305±966)	9.7 (11.7)	3.72-39.6 (4.5-47.9)
BCLC Stage 0	10	1.04/258 (1.26/312)	58.4±98.9 (70.7±120)	9.67 (11.7)	-
BCLC Stage A	67	1.48/5224 (1.79/6322)	281±852 (340±1031)	9.7 (11.7)	3.72-39.6 (4.5-47.9)
Late (Stages B, C and D)	91	1.3/44687 (1.57/54071)	2874±8259 (3478±9994)	119 (144)	5.95-909 (7.2-1100)
BCLC Stage B	26	2.85/34944 (3.45/42282)	1989±7301 (2407±8834)	15.5 (18.8)	5.33-132 (6.45-160)
BCLC Stage C	57	1.3/44687 (1.57/54071)	2313±7079) (2798±8566)	150 (182)	6.14-959 (7.43-1160)
BCLC Stage D	8	557/34531 (674/41782)	9751±15043 (11799±18201)	999 (1209)	-

b) not calculated if sample size is 20 or below

c) In the graphical representation below, this group is designated with an "X"



x ---> X: Control; O: Stage 0; A: Stage A; B: Stage B; C: Stage C; D: Stage D
y ---> AFP (IU/mL)

b) AFP concentration and disease etiology

The AFP concentration as function of etiology for the two patient groups (Control, 1-A to 1-F and HCC, 2-A to 2F) is shown in the following table and graph. All concentrations in the table are in IU/mL and (ng/mL), while concentrations in the graph are in IU/mL. The thick line in the box plots represents the median value.

Label	Etiology d)	N	Min/Max	Mean ±SD	Median	25th-75th perc.
1-A	Cirrhosis	79	0.851/66.9 (1.03/80.9)	4.92±8.59 (5.95±10.4)	2.63 (3.19)	1.85-4.34 (2.24-5.25)
1-B	Hepatitis B	72	1.03/328 (1.25/397)	7.4±38.3 (8.95±46.4)	2.31 (2.79)	1.73-3.11 (2.1-3.76)
1-C	Hepatitis C	27	1.3/6.33 (1.57/7.66)	3.23±1.43 (3.9±1.73)	2.49 (3.01)	2.21-4.73 (2.67-5.73)
1-D	NASH e)	30	1.01/10.9 (1.22/13.2)	3.36±2.36 (4.06±2.86)	2.48 (3.00)	1.74-3.96 (2.11-4.79)
1-E	ALD f)	0	-	-	-	-
1-F	Others	0	-	-	-	-
2-A	Cirrhosis	139	1.04/44687 (1.26/54071)	1536±6096 (1859±7377)	16.6 (20.1)	4.82-320 (5.84-387)
2-B	Hepatitis B	14	2.25/1711 (2.73/2070)	296±536 (358±649)	38.2 (46.2)	-
2-C	Hepatitis C	3	1.86/999 (2.25/1209)	348±564 (421±683)	43.1 (52.1)	-
2-D	NASH	1	-	3.55 (4.3)	-	-
2-E	ALD	2	3.87/33288 (4.69/40278)	16646±23535 (20141±28478)	16646 (20141)	-
2-F	Others	9	1.98/16115 (2.4/19499)	3216±5924 (3891±7168)	210 (254)	-

d) All etiologies except cirrhosis are non-cirrhotic

e) Non-alcoholic steatohepatitis

f) Alcoholic liver disease

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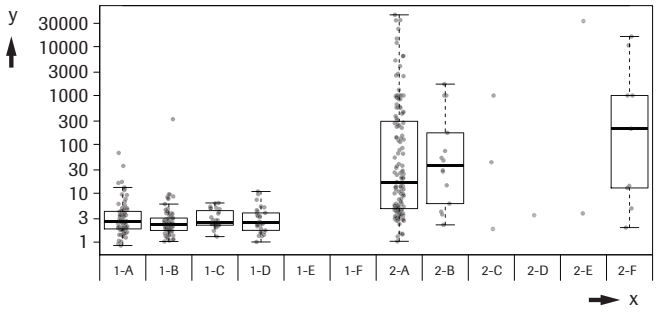


y ---> AFP (IU/mL)

c) Clinical performance of the Elecsys AFP assay in detecting HCC

The sensitivity and specificity of the Elecsys AFP assay in detecting HCC at a cut-off of 165 IU/mL (200 ng/mL) and 16.5 IU/mL (20 ng/mL), and the results of the Receiver Operating Characteristics (ROC) analysis are shown below.

		All HCC	Early Stage HCC[g)]	Late Stage HCC[h)]
AFP cut-off 200 ng/mL	Sensitvity (95 % CI)[i)]	31.5 % (24.6 %, 39.2 %)	15.6 % (8.3 %, 25.6 %)	45.1 % (34.6 %, 55.8 %)
	Specificity (95 % CI)	99.5 % (97.4 %, 100 %)		
AFP cut-off 20 ng/mL	Sensitvity (95 % CI)	51.8 % (44 %, 59.5 %)	36.4 % (25.7 %, 48.1 %)	64.8 % (54.1 %, 74.6 %)
	Specificity (95 % CI)	98.1 % (95.1 %, 99.5 %)		
ROC AUC[j)]		88 % (84.5 %, 91.5 %)	84.5 % (79.3 %, 89.7 %)	90.9 % (86.8 %, 95.1 %)

g) BCLC stages 0, A

h) BCLC stages B,C,D

i) Confidence interval

j) Area under the Curve

d) AFP values in different types of benign and malignant disorders

The following table and graph show the AFP concentration in IU/mL and (ng/mL) in a panel of samples from patients with either a benign liver disease, an immune disorder, or a malignancy other than HCC (N total 397; median age 54 years, 58 % female, 39 % Asian and 61 % Caucasian).

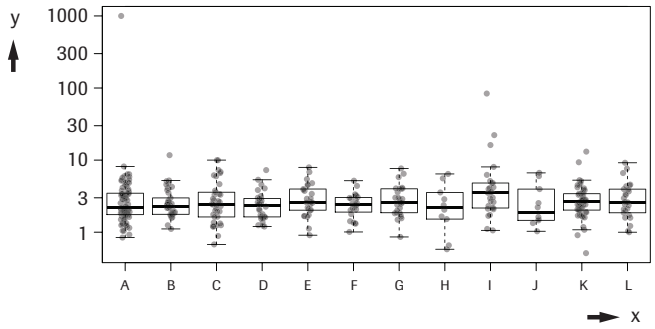
Label	Etiology	N	Min/Max	Mean ± (SD)	Median	25th-75th perc.
A	Benign liver diseases[k)]	87	0.843/999 (1.02/1209)	14.3±107 (17.3±129)	2.20 (2.66)	1.73-3.48 (2.10-4.21)
B	Rheumatoid arthritis	38	1.11/11.7 (1.34/14.2)	2.80±1.84 (3.39±2.22)	2.28 (2.75)	1.77-2.99 (2.14-3.62)
C	Crohn's disease	37	0.676/10.0 (0.819/12.1)	3.21±2.40 (3.88±2.90)	2.42 (2.93)	1.63-3.58 (1.97-4.34)
D	Ulcerative colitis	30	1.20/7.27 (1.45/8.80)	2.58±1.35 (3.12±1.63)	2.37 (2.86)	1.63-2.94 (1.97-3.56)
E	Other autoimmune diseases[l)]	26	0.909/7.93 (1.10/9.60)	3.16±1.72 (3.83±2.08)	2.62 (3.16)	2.02-3.97 (2.44-4.80)
F	Lung cancer	24	1.01/5.18 (1.22/6.27)	2.50±0.978 (3.02±1.18)	2.40 (2.90)	1.90-3.03 (2.30-3.67)
G	Breast cancer	27	0.859/7.67 (1.04/9.27)	3.06±1.60 (3.70±1.93)	2.59 (3.13)	1.85-4.01 (2.24-4.85)
H	Renal cancer	10	0.58/6.43 (0.702/7.78)	2.73±1.96 (3.30±2.37)	2.21 (2.67)	-
I	Cholangio carcinoma	27	1.06/83.8 (1.28/101)	7.48±15.9 (9.05±19.3)	3.51 (4.25)	2.15-4.82 (2.60-5.84)
J	Pancreatic cancer	10	1.03/6.65 (1.25/8.05)	2.83±2.02 (3.43±2.45)	1.92 (2.32)	-
K	Other gastrointestinal cancers[m)]	55	0.512/13.1 (0.62/15.9)	3.00±1.95 (3.63±2.35)	2.68 (3.24)	2.02-3.43 (2.44-4.15)
L	Gynecological cancers[n)]	26	0.999/9.19 (1.21/11.1)	3.24±2.02 (3.92±2.44)	2.62 (3.16)	1.86-3.96 (2.25-4.79)

k) polycystic liver disease, simple cysts, focal nodular hyperplasia, hemangioma, hepatocellular adenoma, non-cirrhotic alcohol liver disease

l) systemic lupus erythematosus, autoimmune thyroiditis

m) colorectal, gastric and esophageal cancer

n) ovarian, endometrial and cervical cancer



y ---> AFP (ng/mL)

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, pooled human sera 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				
Sample	Mean		SD		CV
	IU/mL	ng/mL	IU/mL	ng/mL	%
Human serum 1	2.23	2.70	0.078	0.095	3.5
Human serum 2	1.80	2.18	0.073	0.088	4.1
Human serum 3	5.51	6.67	0.088	0.107	1.6
Human serum 4	16.0	19.4	0.379	0.459	2.4
Human serum 5	156	189	2.81	3.40	1.8
Human serum 6	458	554	7.18	8.69	1.6
Human serum 7	927	1122	17.8	21.5	1.9
PC[o)] Tumor Marker1	7.93	9.60	0.116	0.140	1.5
PC Tumor Marker2	75.0	90.8	1.72	2.08	2.3
PC Universal1	10.8	13.1	0.226	0.273	2.1
PC Universal2	53.9	65.2	1.17	1.42	2.2
PC 1 HCC V2[p)]	3.20	3.87	0.049	0.059	1.5
PC 2 HCC V2[q)]	75.0	90.8	1.14	1.38	1.5

o) PC = PreciControl

p) PC 1 HCC V2 = PreciControl HCC V2, Level 1

q) PC 2 HCC V2 = PreciControl HCC V2, Level 2

Elecsys AFP

cobas®

cobas e 402 and **cobas e** 801 analyzers					
	Intermediate precision				
Sample	Mean		SD		CV
	IU/mL	ng/mL	IU/mL	ng/mL	%
Human serum 1	2.23	2.70	0.084	0.102	3.8
Human serum 2	1.80	2.18	0.076	0.091	4.2
Human serum 3	5.51	6.67	0.133	0.161	2.4
Human serum 4	16.0	19.4	0.441	0.534	2.8
Human serum 5	156	189	3.74	4.53	2.4
Human serum 6	458	554	10.7	12.9	2.3
Human serum 7	927	1122	22.4	27.1	2.4
PC Tumor Marker1	7.93	9.60	0.170	0.206	2.1
PC Tumor Marker2	75.0	90.8	2.23	2.70	3.0
PC Universal1	10.8	13.1	0.271	0.328	2.5
PC Universal2	53.9	65.2	1.40	1.69	2.6
PC 1 HCC V2	3.20	3.87	0.073	0.088	2.3
PC 2 HCC V2	75.0	90.8	1.89	2.29	2.5

Method comparison

a) A comparison of the Elecsys AFP assay, REF 09015124190 (**cobas e** 801 analyzer; y) with the Elecsys AFP assay, REF 07026706190 (**cobas e** 801 analyzer; x) gave the following correlations (IU/mL):

Number of serum samples measured: 188

Passing/Bablok[24]	Linear regression
y = 0.974x - 0.092	y = 0.968x + 0.993
τ = 0.985	r = 0.999

The sample concentrations were between 1.23 and 954 IU/mL.

b) A comparison of the Elecsys AFP assay, REF 09015124190 (**cobas e** 402 analyzer; y) with the Elecsys AFP assay, REF 09015124190 (**cobas e** 801 analyzer; x) gave the following correlations (IU/mL):

Number of serum samples measured: 190

Passing/Bablok[24]	Linear regression
y = 0.986x - 0.121	y = 0.993x - 0.345
τ = 0.991	r = 1.00

The sample concentrations were between 1.08 and 999 IU/mL.

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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

Elecsys AFP

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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

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com
+800 5505 6606

Roche