

REF



SYSTEM

07027079190

07027079501

300

cobas e 402
cobas e 801

English

For use in the USA only

System information

Short name	ACN (application code number)
CEA	10003

Please note

The measured CEA 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 CEA assay method used. CEA 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 CEA assay procedure used while monitoring therapy, then the CEA 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 carcinoembryonic antigen in human serum and plasma. This assay is further indicated for serial measurement of CEA to aid in the management of cancer patients.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

Summary

Carcinoembryonic antigen (CEA) is a highly glycosylated molecule with a molecular weight of approximately 180 kDa.¹ CEA, like AFP, belongs to the group of carcinoembryonic antigens that are produced during the embryonic and fetal period. CEA has been postulated to play a role in a number of biological processes including cell adhesion, immunity and apoptosis.² The formation of CEA is suppressed after birth, and shows a low expression in normal adult tissues.² Therefore only very low CEA levels in the blood of healthy adults can be observed.² The CEA gene family consists of about 17 active genes in two subgroups. The first group contains CEA and the non-specific cross-reacting antigens (NCA); the second group contains the pregnancy-specific glycoproteins (PSG).³ High CEA concentrations are frequently found in cases of colorectal adenocarcinoma.⁴ Slight to moderate CEA elevations can also occur in non-malignant diseases of the intestine, the pancreas, the liver, and the lungs (i.e. liver cirrhosis, chronic hepatitis, pancreatitis, ulcerative colitis, Crohn's Disease).⁵ Smoking can also lead to elevated CEA values and needs to be taken into account when interpreting CEA levels.⁶ CEA determinations are not recommended for cancer-screening in the general population and CEA concentrations within the normal range do not exclude the possible presence of a malignant disease. The main indication for CEA determinations is the follow-up and therapy-management of colorectal carcinoma.

The antigenic determinants of CEA have been characterized, and the available monoclonal antibodies were classified into 5 epitope groups.^{2,7} The antibodies used in the Elecsys CEA assay react with epitopes 2 and 5.

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 6 µL of sample, a biotinylated monoclonal CEA-specific antibody, and a monoclonal CEA-specific antibody labeled with a ruthenium complex⁹ 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)₃²⁺)

Reagents - working solutions

The **cobas e** pack is labeled as CEA.

- M Streptavidin-coated microparticles, 1 bottle, 16.0 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.
- R1 Anti-CEA-Ab~biotin, 1 bottle, 21.0 mL:
Biotinylated monoclonal anti-CEA antibody (mouse/human) 3.0 mg/L; phosphate buffer 100 mmol/L, pH 6.0; preservative.
- R2 Anti-CEA-Ab~Ru(bpy)₃²⁺, 1 bottle, 15.8 mL:
Monoclonal anti-CEA antibody (mouse) labeled with ruthenium complex 4.0 mg/L; phosphate buffer 100 mmol/L, pH 6.5; preservative.

Precautions and warnings

For in vitro diagnostic use.

Exercise the normal precautions required for handling all laboratory reagents.

Disposal of all waste material should be in accordance with local guidelines. Safety data sheet available for professional user on request.

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

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

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



Warning

- H317 May cause an allergic skin reaction.
- H412 Harmful to aquatic life with long lasting effects.

Prevention:

- P261 Avoid breathing dust/fume/gas/mist/vapours/spray.
- P273 Avoid release to the environment.
- 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: 1-800-428-2336

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, K₂-EDTA and K₃-EDTA plasma.

Plasma tubes containing separating gel can be used.

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

Stable for 7 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 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.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- [REF] 11731645322, CEA CalSet, 4 x 1.0 mL
- [REF] 11776452160, PreciControl Tumor Marker, for 4 x 3.0 mL or [REF] 11731416160, PreciControl Universal, for 4 x 3.0 mL
- [REF] 07299001190, Diluent Universal, 36 mL sample diluent
- General laboratory equipment

cobas e analyzer

Additional materials for the **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] 11298500160, 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: This method has been standardized against the 1st IRP WHO Reference Standard 73/601.

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

Quality control

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

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 ng/mL or µg/L).

1 ng/mL CEA corresponds to 16.9 mIU/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	≤ 1130 µmol/L or ≤ 66 mg/dL
Hemoglobin	≤ 0.621 mmol/L or ≤ 1000 mg/dL
Intralipid	≤ 2000 mg/dL
Biotin	≤ 286 nmol/L or ≤ 70 ng/mL
Rheumatoid factors	≤ 1200 IU/mL

Criterion: Recovery ± 1 ng/mL of initial value ≤ 10 ng/mL and ± 10 % of initial value > 10 ng/mL.

Samples should not be taken from patients receiving therapy with high biotin doses (i.e. > 5 mg/day) until at least 8 hours following the last biotin administration.







There is no high-dose hook effect at CEA concentrations up to 200000 ng/mL.

- 3 Thompson JA. Molecular cloning and expression of carcinoembryonic antigen gene family members. *Tumor Biol* 1995;16:10-16.
- 4 Ballesta AM, Molina R, Filella X, et al. Carcinoembryonic Antigen in Staging and Follow-up of Patients with Solid Tumors. *Tumor Biol* 1995;16:32-41.
- 5 Ruibal Morell A. CEA serum levels in nonneoplastic disease. *Int J Biol Markers* 1992;7(3):160-166.
- 6 Fukuda I, Yamakado M, Kiyose H. Influence of Smoking on Serum Carcinoembryonic Antigen Levels in Subjects Who Underwent Multiphasic Health Testing and Services. *J Med Syst* 1998;22(2):89-93.
- 7 Bormer OP, Thrane-Steen K. Epitope group specificity of six immunoassays for carcino-embryonic antigen. *Tumor Biol* 1991;12:9-15.
- 8 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).

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):

	Contents of kit
	Analyzers/Instruments on which reagents can be used
	Reagent
	Calibrator
	Volume for reconstitution
	Global Trade Item Number

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