



CCP



# EliA™ CCP – the Key to Rheumatoid Arthritis Diagnosis

## THE CCP Test

- for quantitative determination of anti-CCP antibodies to aid in the diagnosis of Rheumatoid Arthritis using second generation CCP
- valuable in early arthritis (esp. in cases of Rheumatoid Factor negativity) and as a predictor of severe joint damage (according to recent literature)

## High CLINICAL RELEVANCE

- excellent diagnostic performance in routine use
- high clinical sensitivity and specificity proven in studies with over 2500 samples

## High TECHNICAL PERFORMANCE

- low variances and high reproducibility for consistent results
- high lot-to-lot consistency due to validated, production procedures

## EFFICIENCY also in Calibration

- one curve for all EliA™ IgG tests
- parameter-independent calibration
- stored curve, valid for one month
- combination of different tests in the same run

## EASY handling

- serum as well as plasma can be used
- automated sample dilution
- efficient small run handling



Picture 1: RA-early stage, hands



Picture 2a: RA-late stage, hands



Picture 2b: RA-late stage, x-ray of hands

# Rheumatoid Arthritis

RA is the most common form of inflammatory joint disease and affects 1-2% of the general population, but its diagnosis remains principally a clinical one. The major challenge lies in differentiating RA from the many other forms of arthritis that share several presenting symptoms but vary widely both in outcomes and therapeutic options. The serological marker Rheumatoid Factor (RF) is a well-established analyte but is of limited clinical value due to its poor specificity for RA.

With a growing body of evidence indicating that joint destruction and functional decline in RA are improved by early, aggressive therapeutic intervention, the need for an unequivocal early diagnosis has become critical.

## The Antigen

In the late 1990s it was recognised that antibodies to perinuclear factor (APF), keratin (AKA) and filaggrin were specific for Rheumatoid Arthritis and in 2000, Schelleken's group showed that these antibodies all recognised the same antigen: Cyclic Citrullinated Peptides (CCP). Other groups were able to demonstrate that anti-CCP antibodies are not only highly specific for RA, they also appear early in the disease process when diagnosis is most difficult and intervention most effective. The ELISA based on this work was made commercially available. Two years later a second generation CCP assay with improved performance characteristics was introduced. EliA™ CCP is based on this second generation assay and combines the advantages of a fully-automated system with the well-accepted clinical benefits of this diagnostic and predictive marker.

■ Excellent differentiation from other diseases

## High Clinical Relevance

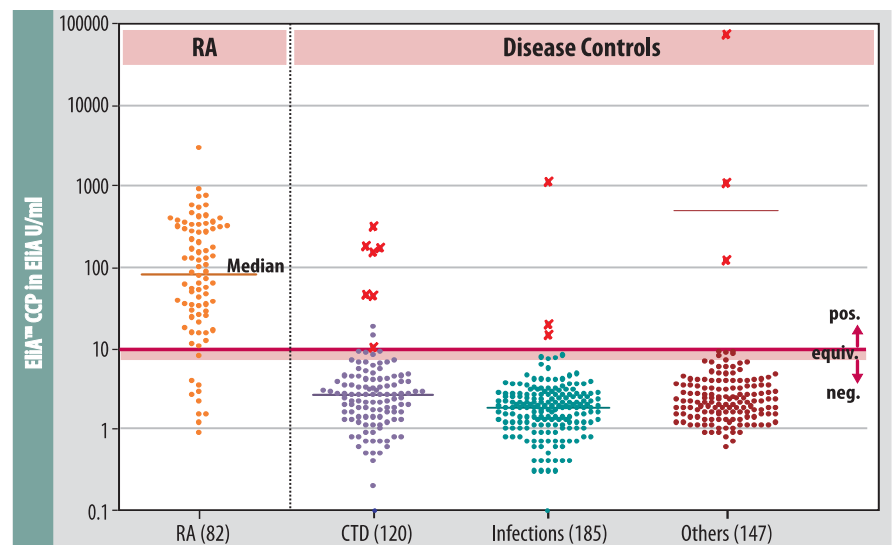


Figure 1: Clinical performance of EliA™ CCP. Disease Controls found positive by EliA™ CCP and confirmed as positive by a reference CCP ELISA are presented with crosses.

The data demonstrate the excellent ability of EliA™ CCP to differentiate RA from CTD like SLE, Sjögren's Syndrome and Mixed Connective Tissue Disease, infections and various other diseases like osteoarthritis.

■ **Excellent clinical sensitivity and specificity**

n = 532 (82 RA, 452 Dis. Contr.)	EliA™ CCP positive > 10 EliA U/ml
Clinical Sensitivity	87.8 %
Clinical Specificity	96.7 %
Positive Predictive Value	82.8 %
Negative Predictive Value	97.8 %
Efficiency	95.3 %

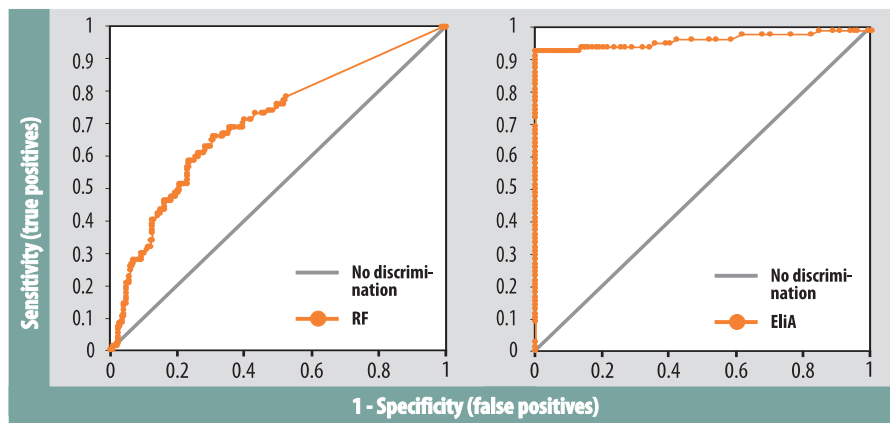
**Table 1:** Clinical performance of EliA™ CCP (in house data)

The results detailed in table 1 and figure 1 demonstrate that EliA™ CCP has an exceptionally good clinical performance as shown in several evaluations. The high sensitivity and specificity result in excellent efficiency and underline the diagnostic relevance of the test.

■ **Outstanding specificity compared to RF**

Study Site	No. of Patients / Controls	Sensitivity of EliA CCP / RF (in %)	Specificity of EliA CCP / RF (in %)
M. Gaubitz, Münster, Germany	185 / 315	68 / 62	96 / 80

**Table 2:** Sensitivity and specificity obtained in routine



**Figure 2:** ROC plot for RF as calculated for RA vs Controls (Mengozi et al)

**Figure 3:** ROC plot for EliA™ CCP as calculated for RA vs Controls (Mengozi et al)

The two studies demonstrate the outstanding better specificity of EliA™ CCP compared to RF. The study by Gaubitz is carried out with routine patients. Pased on clinically well-defined sample panels Mengozzi et al compared ROC (Receiver Operator Characteristics) curves.

■ **Better sensitivity than RF in early RA**

Disease duration	No	RF positive	Anti-CCP positive
< 2 years, early	46	34 (73.9 %)	42 (91.3 %)
> 2 years, late	44	35 (79.5 %)	40 (90.9 %)

**Table 3:** EliA™ CCP and RF in early RA; B. Gilburd et al, Tel Aviv, Israel

The earlier the diagnosis – the better!  
EliA™ CCP supports making up the diagnosis at an early state.

■ **Confirmed value in routine setting**

Study Site	No. of Patients / Controls	Sensitivity (in %)	Specificity
M. Herold, Innsbruck, Austria	66 / 328	80,3	97

**Table 4:** Sensitivity and specificity obtained in routine

The design of the evaluation was chosen in order to evaluate the performance of EliA™ CCP in a routine situation. The high specificity was confirmed. Differences in sensitivity may be due to differences in the patient characteristics in terms of severity and stage of disease.



# The EliA System

## Time for the Essentials

- completely automated (true walk-away, overnight runs)
- predilution option for reduced manual handling
- easy handling and user-friendly operation
- convenient data input
- easy instrument management by custom-made software
- barcode-reader (optional)
- protocols, QC and raw data easily accessible
- optional host link
- detailed QC management

## Cost efficient and flexible

- autoimmunity and allergy on the same instrument
- different autoimmune tests in the same run (puzzle-kit-approach)
- no batching of samples necessary
- once-monthly calibration
- handles primary and secondary tubes
- serum or plasma acceptable
- several ImmunoCAP® Instruments can be linked

## A boost in service for your laboratory and your clinicians

- sample-result turnaround the same day
- small runs can be handled cost-effectively
- detailed documentation of results (patient or requester specific)



## Technical Data

■ <b>Product</b>	EliA™ CCP
■ <b>Shortcut</b>	cp
■ <b>Antigen</b>	2nd generation CCP
■ <b>Standardization</b>	6-point standard curve
■ <b>Cut-off</b>	neg. < 7; pos. > 10 EliA U/ml
■ <b>Measuring Range</b>	0.4 – (at least) 340 EliA U/ml
■ <b>Dilution</b>	1:100 (automated)
■ <b>Sample Material</b>	Serum, Plasma (EDTA, citrate, heparin)
■ <b>Normal Distribution</b>	4.3 / 6.2 EliA U/ml (95 % / 99 % Percentile)
■ <b>Variability in %:</b>	Intra-run (low/medium/high concentration*) 7.0 / 5.1 / 6.6
	Inter-run (low/medium/high concentration*) 2.7 / 2.6 / 5.4

\*for details: see Directions For Use

## Ordering Information

	<i>Package size</i>	<i>Article No.</i>
■ <b>EliA™ CCP</b>	4 x 12	14-5515-01
■ <b>EliA™ CCP Control (neg + pos)</b>	2 x 3	83-1009-01
■ <b>EliA™ Reagents</b>		
EliA™ IgG Conjugate	6 x 48	83-1002-01
EliA™ IgG Conjugate	2 x 48	83-1005-01
EliA™ IgG Calibrator (standard curve)	1 curve	83-1000-01
EliA™ IgG Calibrator Well (Anti-IgG Well)	4 x 12	14-5509-01
EliA™ IgG Curve Control	6	83-1001-01
EliA™ IgG Sample Diluent	6 x 9 ml	83-1003-01
EliA™ Dummy Well	4 x 12	14-5510-01
■ <b>General Reagents</b>		
ImmunoCAP™ Development Kit		10-9263-01
ImmunoCAP™ Washing Solution	5 x 1 l	10-9422-01

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