

EliA™



dsDNA

EliA™
Excellence in Autoimmunity



The EliA™ System

Time for the Essentials

- completely automated (true walk-away, overnight runs)
- easy instrument management by custom-made software
- barcode-reader
- protocols, QC and raw data easily accessible
- optional host link
- detailed QC management
- integrated stock management system on the ImmunoCAP™ 250

Cost efficient and flexible

- autoimmunity and allergy on the same instrument
- different autoimmune tests in the same run
- no batching of samples necessary – small runs can be handled cost-effectively
- once-monthly calibration – curve control each run
- several ImmunoCAP™ instruments can be linked

A boost in service for your laboratory and your clinicians

- sample – result turnaround the same day
- STAT function on ImmunoCAP™ 250 for immediate testing of emergency samples
- overnight runs possible
- detailed documentation of results (patient or requester specific)
- ImmunoCAP™ 100€ – up to 46 determinations in less than 2.5 hours
- ImmunoCAP™ 250 – fully automated random access – up to 350 determinations per shift
- multiple methods in one run
- positive identification and traceability of samples and reagents on ImmunoCAP™ 250



EliA™



EliA™ dsDNA – The Answer in SLE testing

High clinical relevance

- high clinical value supports diagnosis
- optimised for preferential detection of clinically relevant, high avidity antibodies
- high specificity avoids inappropriate follow-up
- standardisation and precision mean reliable monitoring
- correlates well to disease activity – especially lupus nephritis

High technical performance

- low variances and high reproducibility for consistent results
- high lot-to-lot consistency due to validated production procedures
- quantitative results expressed in International Units per ml
- calibrated against WHO reference standard Wo/80

State-of-the-art antigen

- circular, recombinant double-stranded plasmid DNA
- no contaminating ssDNA

Automation

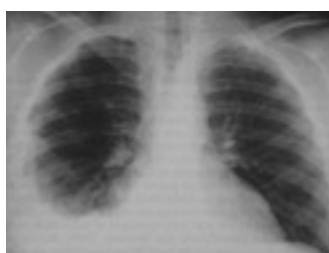
- screen and individual specificity testing available in one run
- choice of ImmunoCAP™ instruments available for low to high throughput
- one stored standard curve to be used with all IgG analytes
- urgent samples can be run cost-efficiently
- easy handling with intuitive software
- serum as well as plasma can be used
- automated sample dilution

Systemic Lupus Erythematosus (SLE)

Systemic Lupus Erythematosus (SLE) represents a classic model for a systemic autoimmune connective tissue disease. The disease affects approximately 40 in 100,000 North Europeans or American Caucasians and the incidence appears to be higher in black populations and even higher in people of Oriental descent. 90% of patients are women and, although there is a genetic component to the disease, the cause remains unknown. SLE can affect virtually all body systems and its severity fluctuates between exacerbations and remissions. Clinical presentation varies among patients and diagnosis may often be one of exclusion and take a long period of time to be firmly made. Symptoms can include fatigue, fever, anorexia, nausea and weight loss as well as a host of organ-specific signs depending on the course in each patient. Skin, musculoskeletal, renal, neurological, cardiopulmonary and vascular features represent more serious manifestations.



Picture 1: SLE, Butterfly rash



Picture 2: SLE, pleural effusions in lung x-ray

Disease Markers

More than 80% of sera from patients with SLE contain antibodies to double-stranded dsDNA which are considered to be a highly specific marker, representing one of the American College of Rheumatology (ACR) diagnostic criteria for the disorder. There is increasing evidence showing that high-avidity antibodies are more clinically relevant in SLE. Additionally, the accurate quantitation of dsDNA antibodies can be used as a tool to monitor the clinical course of a defined SLE patient, as a clear relationship exists between anti-dsDNA levels and disease activity. Antibodies to dsDNA are a heterogeneous group and may vary considerably in terms of avidity, complement fixing ability, cross-reactive patterns and other binding characteristics. Different assay systems detect different subpopulations of these autoantibodies so will not always agree.

■ Specific marker for SLE

■ Recombinant antigen for best quality, consistency and performance

EliA™ dsDNA

In the context of DNA, only the antibodies to double-stranded DNA are specific for SLE so it is crucial that the antigen preparation does not contain any ssDNA, histones or any other proteins which might give false positive results. EliA™ dsDNA wells are coated with circular double-stranded recombinant plasmid DNA to avoid the possibility of contaminating antigens while, at the same time, ensuring that the antigenic conformity of the preparation remains true to the native, double-stranded form. The antigen-antibody reaction is performed under conditions to further increase clinical specificity and limit the formation of bonds by low-avidity antibodies.

For EliA™ dsDNA, once-monthly calibration is required and consistency is checked by a one point curve control in each run. The system is fully automated from sample dilution to result interpretation and avoids the technical issues related to assays using either radioactivity or immunofluorescence.

Production of the recombinant antigen using GMP and ISO controlled conditions allows us to manufacture large batches and to guarantee high lot-to-lot consistency so that patient antibody levels can be accurately monitored over long periods of time to give the most clinically useful information about the disease activity status.

High Clinical Relevance

■ **Highly specific and quantifiable**

EliA™ dsDNA is designed to give good clinical performance in diagnosis and monitoring of SLE. This has been demonstrated in many publications describing its use on the ImmunoCAP™ 100 instrument and now, because of the excellent system correlation achieved, the same level of performance is available on the higher throughput ImmunoCAP™ 250 system.

| | | EliA™ | Farr-RIA | CLIFT |
|-----------------|----------------------------------|-------|----------|-------|
| Sensitivity (%) | SLE | 39.5 | 31.6 | 13.2 |
| Sensitivity (%) | Active SLE | 70.8 | 66.7 | 29.2 |
| Sensitivity (%) | SLE nephritis | 55.0 | 50.0 | 25.0 |
| Specificity (%) | Control Group non-SLE AI disease | 93.2 | 96.1 | 99.0 |

Table 1: Diagnostic sensitivity of different methods (Hernando et al 2002; Clin Chem Lab Med 40(10): 1056-1060)

■ **Good correlation to disease activity**

The results detailed in table 1 show the excellent clinical performance of EliA™ dsDNA when compared to other, established methods. In particular, note the high sensitivity achieved in active SLE. This study utilised as controls, patients with other autoimmune disorders and positive antinuclear antibody (ANA) test results.

In another study, EliA™ dsDNA was compared to a radioimmunoassay (FARR) in assessing the changes in titres in sera from SLE patients according to the clinical status and treatment. The authors found that the anti-dsDNA levels measured were significantly related and that EliA performed similarly to the Farr test for follow-up of SLE patients. One patient's data is illustrated below.



Figure 1: Patient A – Comparison of the anti-dsDNA Ab kinetics (Lakaf et al, 2002, 6th Dresden Symposium on Autoantibodies)

The decrease in titer with remission as well as the increase which correlates to a worsening of disease symptoms is clear in both the FARR and EliA™ assay results.

Standardised, broad measuring range

■ **Calibrated against WHO standard**

Because patients, clinicians and samples are more mobile now than ever before, and because dsDNA antibody levels are used to determine disease activity, standardisation of the assay has become crucial. EliA™ dsDNA is standardised against the World Health Organisation (WHO) standard Wo/80 which gives a linear dilution response over the applicable measuring range. Changes in antibody level signifying remission or the onset of symptom exacerbation can be clearly seen in the system which uses a 6 point standard curve to maximise the accuracy of results and has a measuring range from 0.5 IU/ml to at least 400 IU/ml.

Technical Data

| | |
|------------------------------|---|
| ■ Product | EliA™ dsDNA |
| ■ Antigen | circular, double-stranded recombinant plasmid DNA |
| ■ Standardisation | World Health Organisation standard Wo/80 |
| ■ Cut-off | neg. <10 IU/ml; equiv. 10–15 IU/ml; pos. >15 IU/ml |
| ■ Measuring Range | 0.5 IU/ml – at least 400 IU/ml |
| ■ Dilution | 1:10 (automated) |
| ■ Sample Material | Serum, Plasma (EDTA, citrate, heparin) |
| ■ Normal Distribution | Mean 2.4IU/ml, 95 th percentile 6.3 IU/ml) |
| ■ Reproducibility | Intra-run CV* 2.8–5.3 % Inter-run CV* 2.8–4.6 % |

*for details see Directions For Use

Ordering Information

| | <i>Package size</i> | <i>Article No.</i> |
|--|---------------------|--------------------|
| ■ EliA™ dsDNA Well | 4 x 12 | 14-5500-01 |
| ■ EliA™ ANA Control (neg + pos) | 2 x 3 | 83-1004-01 |
| ■ EliA™ IgG Calibrator Well (Anti-IgG Well) | 4 x 12 | 14-5509-01 |
| ■ EliA™ 100 Reagents | | |
| EliA™ IgG Conjugate | 6 x 48 | 83-1002-01 |
| EliA™ IgG Conjugate | 2 x 48 | 83-1005-01 |
| EliA™ IgG Calibrator | 6 vials | 83-1000-01 |
| EliA™ IgG Curve Control | 6 vials | 83-1001-01 |
| ■ EliA™ 250 Reagents | | |
| EliA™ IgG Conjugate 50 | 6 x 50 | 83-1017-01 |
| EliA™ IgG Conjugate 200 | 6 x 200 | 83-1018-01 |
| EliA™ IgG Calibrator Strips | 5 strips | 83-1015-01 |
| EliA™ IgG Curve Control Strips | 5 strips | 83-1016-01 |
| ■ General Reagents – ImmunoCAP™ 100 | | |
| ImmunoCAP™ Development Kit | | 10-9263-01 |
| ImmunoCAP™ Development Solution | 6 x 48 | 10-9478-01 |
| ImmunoCAP™ Stop Solution | 6 x 240 | 10-9479-01 |
| ImmunoCAP™ Washing Solution | 6 x 1 l | 10-9422-01 |
| ■ General Reagents ImmunoCAP™ 250 | | |
| ImmunoCAP™ Development Solution | 6 x >170 | 10-9440-01 |
| ImmunoCAP™ Stop Solution | 6 x 590 | 10-9442-01 |
| ImmunoCAP™ Washing Solution | 2 x 5 l | 10-9202-01 |

Order No. 91 51 500 Freiburg 10/2006

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