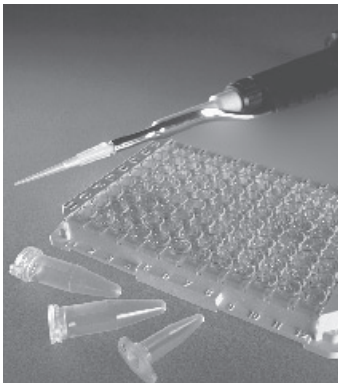
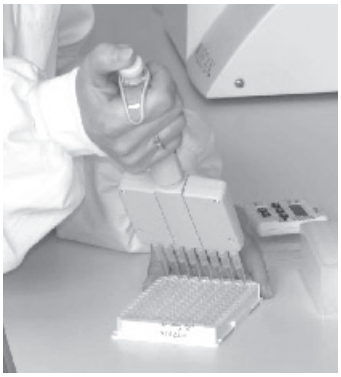
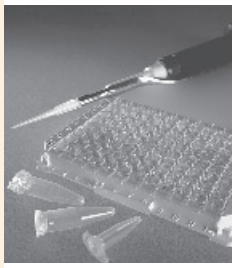
Varelisa™





PR3 ANCA
MPO ANCA

EliA™
Excellence in Autoimmunity



The Varelisa™ System

Well-established and reliable

- system introduced in 1994
- FDA cleared and CE labelled
- well represented in major international quality surveys

Automation solved

- CE-labelled package of Varelisa™ assays + Dynex DSX instrument
- automation-friendly reagents
- customised solutions available

Convenient and time saving

- ready-to-use sample diluent, conjugate, substrate, calibrators and controls
- one standard protocol for almost all assays for efficient parallel testing
- easy archiving of electronic directions for use for documentation and accreditation
- all reagents barcoded
- Lockwell™ break away format allows assaying individual patients

Quality in the focus

- production according to GMP guidelines
- ISO certification since 1997
- high lot-to-lot consistency from standardised production procedures

Global network for local service and support

- serum test service
- literature service
- Phadia scientific symposia
- scientific EliA™ Journal

PR3 and MPO Assays on the Varelisa™ Platform – Surer Diagnosis of ANCA-Associated Vasculitides

High clinical relevance

- high specificity avoids false positive results
- high positive predictive values for clinically more helpful results
- performance proven with more than 260 clinically defined patient samples
- cut-offs clinically evaluated
- quantitative results for accurate assessment

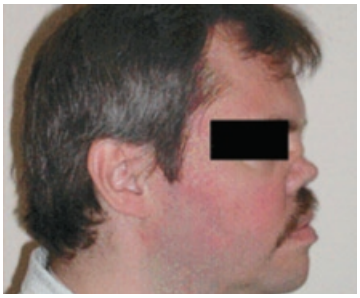
Varelisa™ PR3 capture – no longer available

High technical performance

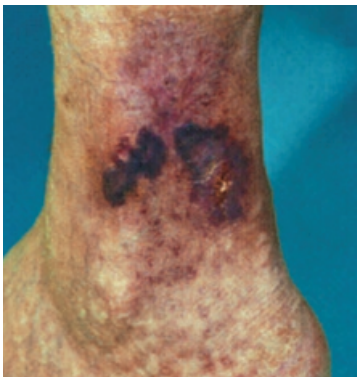
- low variances and high reproducibility for consistent results
- high lot-to-lot consistency from validated production procedures
- results expressed as U/ml based on a six-point standard curve
- large lot sizes – fewer revalidations necessary

Easy handling

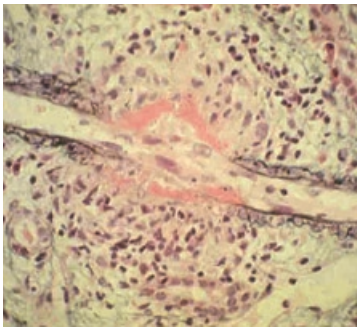
- ready-to-use reagents where possible
- serum or plasma can be used
- convenient incubation times
- ready for automation on microplate processors



Picture 1: *Saddle nose in Wegener's granulomatosis*
(picture kindly provided by Dr. W. Schmitt, University of Heidelberg, Germany)



Picture 2: *Vasculitis in legs*
(picture kindly provided by Dr. W. Schmitt, University of Heidelberg, Germany)



Picture 3: *Histological picture of vasculitis*
(picture kindly provided by Dr. D. Jayne, Addenbrooke's Hospital, Cambridge, UK)

ANCA-Associated Vasculitides

‚Vasculitis' is the term used for inflammatory diseases that involve blood vessel walls and the surrounding interstitium. It may affect the large, medium, or small blood vessels. Small-vessel vasculitis may be further classified as antineutrophil cytoplasmic antibodies (ANCA)-associated or non-ANCA-associated vasculitis. The variety of clinical presentations associated with the many aetiologies of vasculitides makes the diagnosis of specific forms of vasculitis difficult. This is important, as some vasculitides with similar clinical presentation have very different prognoses and are treated differently.
ANCA-associated vasculitides are the most common primary systemic small-vessel vasculitides to occur in adults and belong to the most severe vasculitides with the worst prognosis. About 75% of all vasculitis cases are ANCA positive with patients showing antibodies to MPO (myeloperoxidase) or PR3 (proteinase 3). They include microscopic polyangiitis (MPA), Wegener's granulomatosis (WG), and Churg-Strauss syndrome (CSS). Treatment is quite aggressive and usually includes corticosteroid and immunosuppressive therapy.

The Antigens

The only antigens relevant for the diagnosis of ANCA-associated vasculitides are proteinase 3 and myeloperoxidase. Both are enzymes located in the azurophilic granules of neutrophil granulocytes and are involved in pathogen defense.
The antigens used for the Varelisa™ PR3 ANCA and Varelisa™ MPO ANCA are highly purified proteins from human granulocytes.

Antibodies Against PR3 and MPO in the Diagnosis of Vasculitides

PR3 ANCA is the typical antibody in WG and is found in 65-75% of cases, depending on disease activity and the method used. MPO ANCA are a marker for MPA (frequency >50%) but also occur in about 40% of CSS. However, MPO ANCA may also be present in WG and anti-PR3 in MPA and CSS, although to a much lower extent. In particular, PR3 ANCA have proven to be useful predictors of relapses.

High Clinical Relevance

- **Excellent correlation with clinical data**

All ANCA assays were clinically evaluated with large panels of clinically defined samples: 130 – 152 ANCA associated vasculitides (WG, MPA, CSS, necrotizing crescentic glomerulonephritis) and 115 – 256 disease controls (connective tissue diseases, inflammatory bowel diseases, infections and others).
Both Varelisa™ PR3 ANCA and Varelisa™ MPO ANCA show a very high specificity of 99.6 and 96.5 %, respectively. A high specificity is of major importance, because the risk for false positive results should be kept as low as possible, particularly in ANCA-associated vasculitides which need a prompt and aggressive treatment. Both Varelisa™ ANCA tests exhibit a good sensitivity for vasculitis patients at the time of diagnosis. Their outstanding specificity and the possibility of obtaining quantitative results in the first measuring step make these assays excellent tools to support the clinical findings in the diagnostic process.

Technical Data

Products	Varelisa™ PR3 ANCA Varelisa™ MPO ANCA
Antigens	Proteinase 3 and myeloperoxidase, purified from human granulocytes
Isotype	Immunoglobulin G, IgG
Standardisation	6-point standard curve; results in U/ml
Cut-off	neg. < 6 U/ml; equivocal 6 – 9 U/ml; pos. >9 U/ml
Measuring range	Varelisa™ PR3 ANCA: 0.5 – 100 U/mlml Varelisa™ MPO ANCA: 1.0 – 100 U/ml
Dilution	1:101
Sample material	Serum, Plasma (EDTA, heparin, citrate)

Reproducibility

	intra-	and	inter-assay CV in %
Varelisa™ PR3 ANCA	4.8 – 5.9		2.4 – 9.3
Varelisa™ MPO ANCA	4.8 – 9.5		3.5 – 10.7

Ordering Information

	Package size	*Article No.*
Varelisa™ PR3 ANCA	96 determinations	17796
Varelisa™ MPO ANCA	96 determinations	17696

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Order No. 91 01 178 Freiburg 08/2006