Biomarkers for Alzheimer testing in routine

INNOTEST® immunoassays for the quantification of β-amyloid (1-42), β-amyloid (1-40), total tau and phospho-tau (181P) in cerebrospinal fluid

** ORDERING INFORMATION **

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>PRODUCT DESCRIPTION</th>
<th>ARTICLE NO.</th>
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<tr>
<td>INNOTEST® β-AMYLOID (1-42) 96 tests/kit</td>
<td>-IVD</td>
<td>81576***</td>
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<tr>
<td>Aβ (1-42) CAL-RVC pack</td>
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<td>Aβ (1-42), HS Con</td>
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<td>INNOTEST® hTAU Ag 96 tests/kit</td>
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<td>Tau Ag CAL-RVC pack</td>
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<td>INNOTEST® PHOSPHO-TAU(181P) 96 tests/kit</td>
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*** A license for the use of amyloid beta monoclonal antibodies contained in this product under patents US 6114133, US7811769, and EP 0792458 has been obtained from Eli Lilly and Company.

The next step for INNOTEST® Alzheimer assays

- Ready-to-use calibrators
- Reduced inter- and intra-run variation
- Assay run validation
- Generic and color-coded reagents
- Easier test automation
- CE mark of INNOTEST β-AMYLOID (1-42)
Single-analyte assays using ELISA technology

**Clinical Background**

Alzheimer’s disease (AD) is the most common form of dementia and is histologically characterized by the accumulation of extracellular amyloid plaques and intracellular neurofibrillary tangles throughout the brain. The major constituents of amyloid plaques are the β-amyloid peptides consisting of 40 and 42 amino acids, which are derived from the amyloid precursor protein. Neurofibrillary tangles are made up of paired helical filaments consisting of hyperphosphorylated tau protein (phospho-tau). Tau protein, present in the brain in 6 different isoforms, is an intracellular protein that is released upon neuronal death.

**Intended Use**

The INNOTEST® assays described here are solid-phase enzyme immunoassays for the quantitative determination of β-amyloid(1-42), total tau and phospho-tau in human cerebrospinal fluid (CSF). The combined use of these markers allows identification of AD pathology ante-mortem.

**Products**

INNOTEST® β-AMYLOID (1-42)

INNOTEST® β-AMYLOID (1-40)

INNOTEST® hTAU Ag

INNOTEST® PHOSPHO-TAU (181P)

**Assay Principle**

The INNOTEST® assays for the quantitative determination of β-amyloid(1-42), total tau and phospho-tau in human cerebrospinal fluid (CSF) can be used in clinical routine to discriminate AD from normal aging, other neurological diseases and other types of dementia (non-AD). Interpretation of the results, however, should always be done in combination with other clinical information.

**Assay Features**

- **Calibrator range**: 62.5 - 4000 pg/mL, 7,8 - 1000 pg/mL, 50 - 2500 pg/mL, 15,6 - 1000 pg/mL
- **Calibrator and Run Validation Controls (ready-to-use)**: 6 + 2
- **Sample volume**: 25 µL
- **Dilution**: Not applicable
- **Assay duration**: Approx. 3h (3h sample incubation), Approx. 7h (overnight sample incubation)

**Assay Advantages**

- Simple colorimetric immunoassays, standard technology
- Easily automated on microplate processor (generic components)
- Reference assays for CSF testing in routine, supported by many peer-reviewed scientific publications
- Less than 300 µL of CSF necessary for determination of complete biomarker profile
- CE-mark for all INNOTEST Neuro assays: suitable for in vitro diagnostic use
- Excel macro available for consistent concentration calculation

**Features of innotest® Products**

Run Validation Controls (RVC)

Validation of test runs:
- General test performance
- Correctness of the standard curve

Facilitates lab accreditation

Ready-to-use calibrators (RTU CAL)

Ease of use, less chance of errors

Reduction of variation:
- Inter-run, intra-lab variation
- Inter-lab variation

**Generic and color-coded components**

Interchangeable components between all INNOTEST β-amyloid and tau assays are: Sample Diluent, Wash Solution, Substrate, Substrate Buffer and Stop Solution:
- Easier test automation
- Color-coded reagents: Conjugate Diluent 1 and 2:
  - Easy recognition of different components

**Knowledge of a patient’s AD biomarker profile increases diagnostic certainty for the clinician.**

Biochemically based diagnosis is probable long before the clinical symptoms of AD are fully manifest.*

In patients with a discrepancy between CSF phospho-tau(181P) and CSF β-amyloid(1-42), the assessment of the β-amyloid(1-42)/β-amyloid(1-40) ratio leads to a 50% reduction in the number of indeterminate profiles.**

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*Running two tests is recommended
**CAL 1 and CAL 2 can be removed from the calibration curve without impact on the concentration determination.