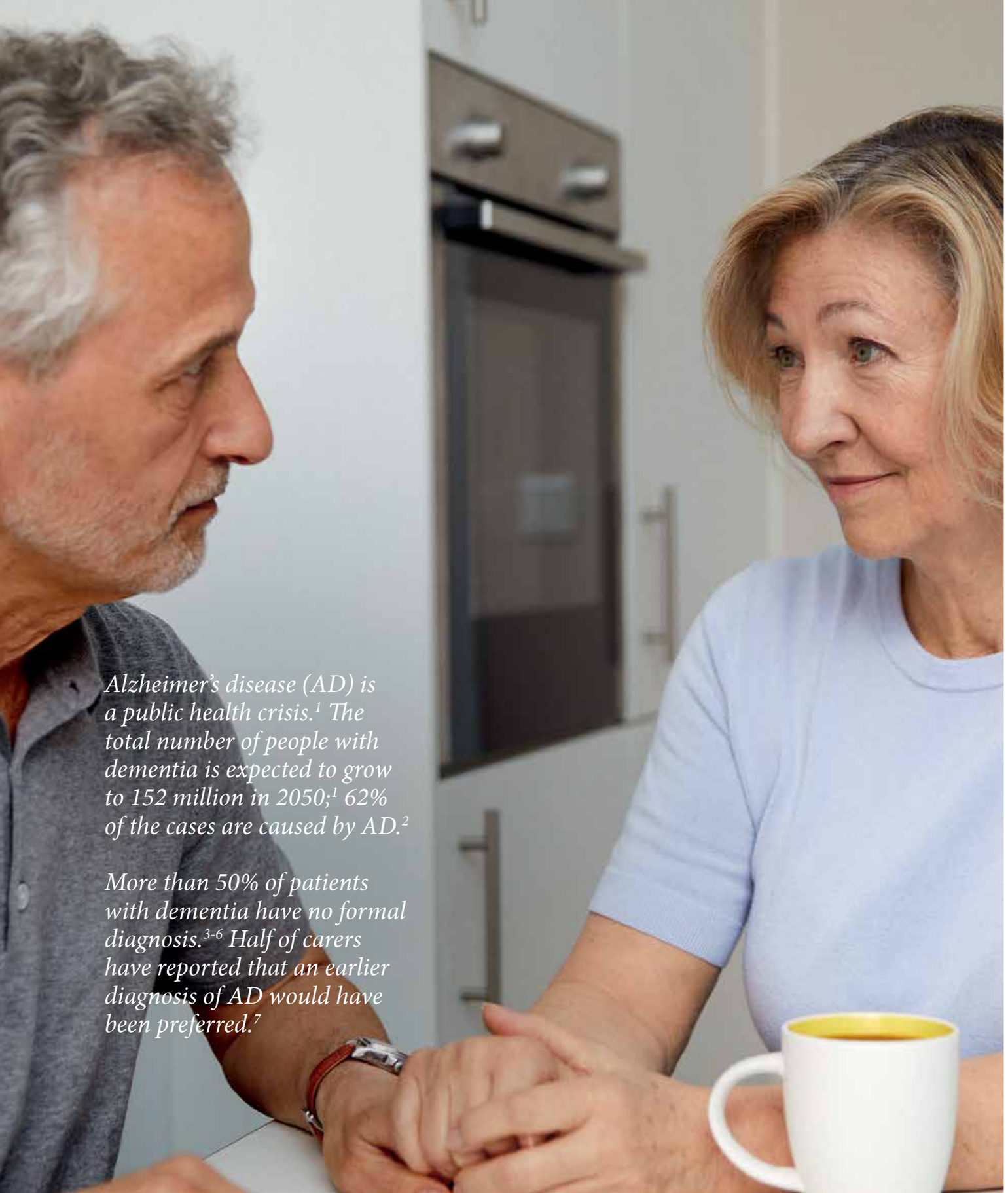
The Power of Elecsys® in Alzheimer's disease

Robust and accurate biomarker tests to solve clinical questions



Alzheimer's disease (AD) is a public health crisis.[1] The total number of people with dementia is expected to grow to 152 million in 2050;[1] 62% of the cases are caused by AD.[2]

More than 50% of patients with dementia have no formal diagnosis.[3-6] Half of carers have reported that an earlier diagnosis of AD would have been preferred.[7]

The Power of Early Diagnosis

Patients want to know if their symptoms are due to AD.[8]

Confirming a diagnosis is important as it can reduce anxiety and may provide a sense of reassurance to patients and families that their symptoms are finally given a name.[9]

Early diagnosis allows for appropriate and timely intervention.[11]

Approximately 35% of risk factors can be modified to delay or prevent Mild Cognitive Impairment (MCI) and AD.[12] When individuals receive an early diagnosis, they can:[12]

Early diagnosis can bring substantial cost-savings for healthcare systems.[10]

An early diagnosis of AD is not only a relief for patients and their loved ones, but it can also benefit wider society.[10]

A recent study run by the Alzheimer's Association revealed that an early diagnosis at MCI stage couldpotentially save up to USD 7.9 trillion in USA alone.[10]

- Plan for financial support and care
- Manage comorbidities i.e. hypertension
- Treat symptoms with medication
- Begin health measures i.e. physical exercise

The Power of Biomarkers

Historically AD diagnosis was confirmed post-mortem through brain autopsy.[13] Clinical diagnosis had modest performance and provides no information on histopathological causes of AD.[14]

In the last decade, it became clear that amyloid and tau accumulation are the key pathological features of AD.[15] The accumulation start 15 years prior to symptoms onset.[16,17]

Biomarkers are recommended for AD diagnosis and clinical trial enrolment.[18-20]

- The National Institute on Aging and Alzheimer's Association (NIA-AA) has recently recommended the use of biomarkers to measure the continuum of AD and support with diagnosis.[18]
- The US Food and Drug Administration (FDA) and European Medicine Agency (EMA) now accept biomarker change as an endpoint of clinical trials in early stage of AD.[19,20]

Biomarkers enhance diagnostic accuracy and physician confidence.[21]

In 2019, the Imaging Dementia Evidence for Amyloid Scanning (IDEAS) study published the first results showing that, by adding amyloid biomarkers like amyloid PET to the patient clinical assessment, diagnostic accuracy markedly improves.[21]

IDEAS study results[21]

60%

The use of amyloid PET was associated with changes in clinical management for over 60% of patients with MCI and AD within 90 days.

+ PET scans

Positive amyloid PET scans led to new diagnosis of AD in nearly half of patients who were not previously diagnosed with AD.

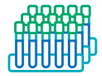
– PET scans

Negative amyloid PET scans led physicians to rule out AD for approximately one in three patients who had been previously been given an AD diagnosis.

Automated CSF solutions support routine implementation of biomarkers.[22]

CSF biomarkers were traditionally measured through manual ELISA assays. Manual assays had several implementation hurdles that prevented wide adoption of CSF markers.[22]

Automated solutions provide an efficient alternative to manual assays by:[22]

Automated analysers		Manual assays
Automated analyzers are proposed to have better repeatability and intermediate precision		High lot to lot and between lab variability due to differences in analytical procedures and analytical techniques determining a low precision and reliability of the results generated
No incubation time required. Turnaround time to result is 18 – 30 minutes		Long incubation times leading to long turnaround time to result (several weeks)
No batch testing required*		As most assays are based on the 96-well plate immunoassay format, laboratories were forced to perform batch testing to justify the analysis financially and determining a longer turnaround time to result.

**Dependent on volume of testing of each single lab*

Automated solutions represent a more suitable option for clinical routine implementation of CSF biomarkers.

The Power of Elecsys®

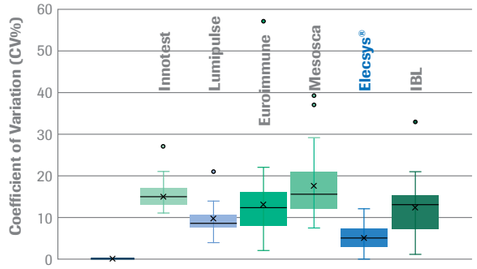
The Elecsys® AD CSF portfolio includes three assays:[23]

- **Elecsys® β-Amyloid (1-42) CSF II (AB42 2) immunoassay**
- **Elecsys® Phospho-Tau (181P) CSF (pTau) immunoassay**
- **Elecsys® Total-Tau CSF (tTau) immunoassay**

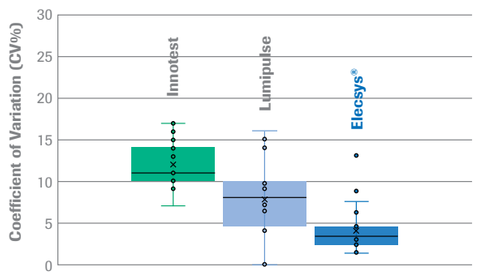
Your results are reliable with Elecsys®.[23]

Elecsys® AD portfolio achieve highly accurate and precise ① results across all **cobas** e platforms.[23] The precision of Elecsys® is also confirmed in the Alzheimer's Association Quality Control (AAQC) program.[24]

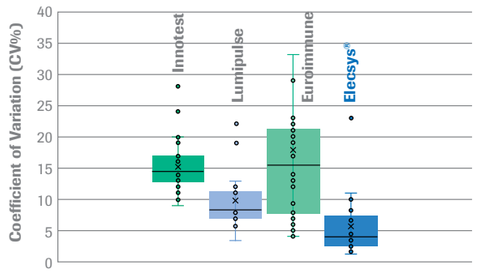
CV% for Manual and automated CSF assays AAQC rounds (2014-2020)



Biomarker: β-Amyloid (1-42)[40]



Biomarker: Phosphorylated Tau[40]



Biomarker: Total Tau[40]

AAQC results (2014-2020). The box whiskers plot in green identify manual assays, whilst the blue ones the automated assays.[40]

The linearity across a broad measuring range plus reagent and calibrator stability facilitate accurate results.[23] ②

Testing of AD parameters becomes fast and fully integrated on cobas e automated platforms.[23]

Elecsys® assay design allows a targeted and fast quantification of AD parameters with a turnaround time of only 18 minutes.[23] ③

Elecsys® Abeta42 2, pTau and tTau are available on all **cobas e** instruments, making AD testing possible for every laboratory size.[23] ④

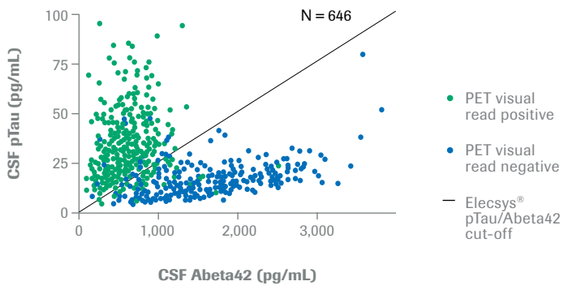
With Elecsys® and **cobas®** technology, manual work is reduced through integration into lab automation.[23] ⑤

	Elecsys® AB42 2 CSF assay	**Elecsys® pTau CSF assay**	**Elecsys® tTau CSF assay**
Testing time	18 minutes ③		
Test principle	Sandwich principle ③ ⑤		
Calibration	2 point ⑤		
Traceability	*Traceability:* This method has been standardized against the three certified reference materials (CRMs), ERM-DA480/ IFCC,ERM-DA481/IFCC and ERM-DA482/IFCC.	This method has been standardized against a purified reference material Tau(172-205) [pThr181] amide, absolutely quantified via amino acid analysis (AAA).	This method has been standardized against a reference method. Calibrator values are based on weighted purified reference tTau material, traceable to NIST amino acid reference calibrators.
Sample material	Human Cerebrospinal Fluid		
Sample volume ***cobas*** *E1G* ***cobas*** *E2G*	50 µL 30 µL		
Onboard stability ***cobas*** *E1G* ***cobas*** *E2G*	28 days ⑤ 16 weeks		
Measuring range	150 - 2,500 pg/mL ②	8 - 120 pg/mL	80 - 1,300 pg/mL
Limit of Blank (LoB)	50 pg/mL	4 pg/mL	30 pg/mL
Limit of Detection (LoD)	100 pg/mL	8 pg/mL	60 pg/mL
Limit of Quantitation (LoQ)	150 pg/mL	8 pg/mL	80 pg/mL
Precision	**cobas e** 601, **cobas e** 602: 4.1% – 7.0% (7.28 – 148 pg/mL) ① **cobas e** 411: 3.6% – 9.2 % (6.71 – 192 pg/mL) ④	**cobas e** 601, **cobas e** 602: 1.5 – 3.2% (0.410 – 0.662 pg/mL) **cobas e** 411: 1.6 – 2.5% (0.502 – 0.539 pg/mL)	**cobas e** 601, **cobas e** 602: 4.4 – 5.6% (13.7 – 59.6 pg/mL) **cobas e** 411: 5.9 – 7.2% (18.8 – 74.6 pg/mL)
	cobas e 801: 1.6% – 5.9% (2.44 – 126 pg/mL) ⑤ **cobas e** 402: 1.0% – 2.0% (1.70 – 42.1 pg/mL)	**cobas e** 801: 1.3 – 2.6% (0.343 – 2.86 pg/mL) **cobas e** 402: 1.2 – 2.5% (0.325 -0.532 pg/mL)	**cobas e** 801: 1.0 – 1.3% (0.965 – 13.9 pg/mL) **cobas e** 402: 1.6 – 1.9% (1.61 – 6.53 pg/mL)

Elecsys® AD CSF assays can detect amyloid positivity, enhancing diagnostic accuracy and physician confidence.[21,25]

Elecsys® AD CSF assays are concordant to amyloid PET and provide an alternative solution for detection of amyloid positivity.[24,25]

Distribution of pTau and Abeta42 CSF biomarkers colored by PET visual read classification[24,25]



Elecsys® ratios (pTau/Abeta42, tTau/Abeta 42) achieve 90% concordance with amyloid PET. A result above the cut-off is consistent with a positive PET visual read.[24,25]

Performance of CSF biomarkers cut-offs versus amyloid PET visual read[24,25]

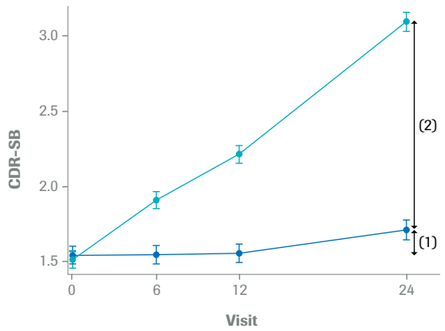
	Cut-off (+)	Cut-off (-)	PPA,%	NPA, %	OPA, %
Elecsys® pTau/AB42 2	>0.023	≤0.023	90.9 (83.9–95.6)	89.2 (83.5–93.5)	89.9 (85.7–93.2)
Elecsys® tTau/AB42 2	>0.28	≤0.28	90.9 (83.9–95.6)	89.2 (83.5–93.5)	89.9 (85.7–93.2)

Note: Values in brackets are 95% confidence intervals

Elecsys® AD CSF assays enable early diagnosis and intervention by identifying patients with MCI at risk of progression to AD.[25]

Identification of disease progression is key for planning patient treatment and care.[26] Elecsys® ratios (pTau/AB42 2 tTau/AB42 2) aid to identify adult subjects with MCI at higher vs lower risk of cognitive decline as defined by change in clinical score within 2 year period.[24,25]

Model-based average ± standard error in biomarker-negative (blue) and biomarker-positive (aqua) CDR-SB for follow-up at 0, 6, 12, and 24 months.[24,25] A higher CDR-SB score implies a worsening of the patient's cognitive function.



Validated clinical cut-offs ensure an easier implementation of Elecsys® in your lab.[22,25]

Universal cut-offs concentrations are already applied for many biomarkers in clinical routine (i.e. HbA1c in diabetes mellitus).[22] The next step is to apply the same concept for AD biomarkers to ensure universal interpretation of results.[22]

Elecsys® AD CSF assays have clinically validated cut-offs, that allow easier adoption by the lab and between lab comparison.[22,25]

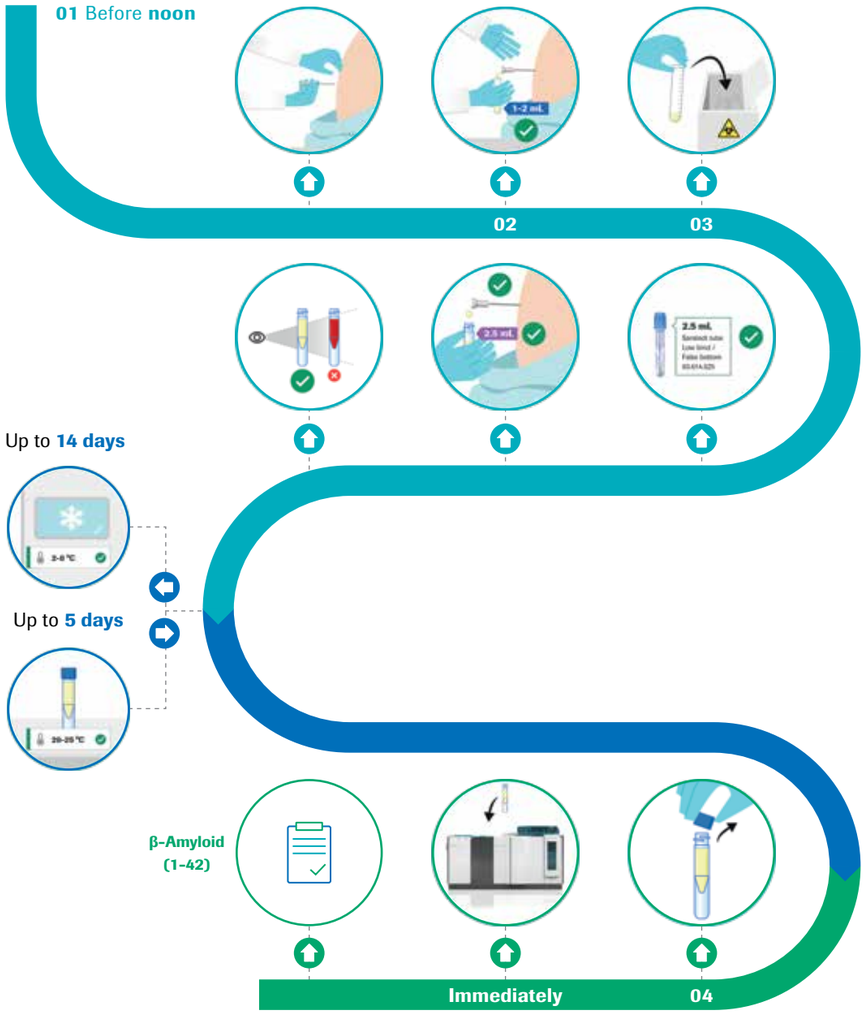
	Cut-off (+)	Cut-off (-)
AB42 2	≤ 1030 pg/mL	> 1030 pg/mL
pTau	> 27 pg/mL	≤ 27 pg/mL
tTau	> 300 pg/mL	≤ 300 pg/mL
pTau/AB42 2	> 0.023	≤ 0.023
tTau/AB42 2	> 0.28	≤ 0.28

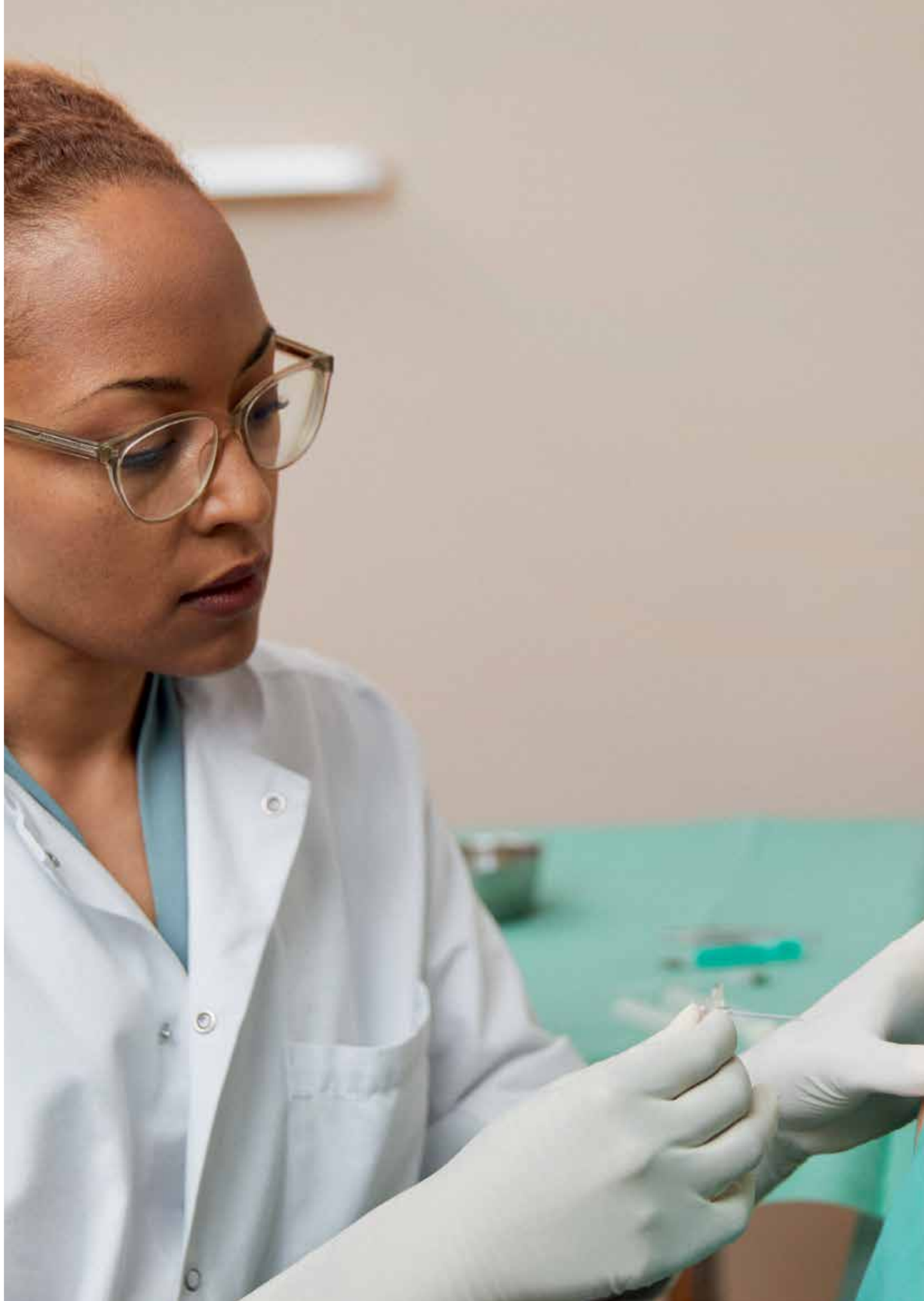
The high reproducibility of Elecsys® support the establishment of robust cut-off values that are valid worldwide.[22,25]

Elecsys® pre-analytical protocol allows for reduction of variability between sites, improvements in the accuracy of biomarker measurement and inter-lab comparison.[23,27]

CSF biomarker, and Abeta42 in particular, are highly influenced by pre-analytical handling including tube type, collection volume, transport conditions…[27]

Elecsys® AD CSF assays have a validated protocol designed to minimize pre-analytical variations.[23,27]





Ordering information

Product	Material configuration	Material Number
Elecsys® β-Amyloid (1-42) CSF II[a)]	60 tests	08 821 909 190
Elecsys® β-Amyloid (1-42) CSF II[b)]	100 tests	08 821 941 190
Calset β-Amyloid (1-42) CSF II	4 x 1.0 mL	08 821 976 190
PreciControl β-Amyloid (1-42) II	6 x 1.0 mL	08 821 968 190
Elecsys® Phospho-Tau (181P) CSF[a)]	60 tests	08 846 693 190
Elecsys® Phospho-Tau (181P) CSF[b)]	100 tests	08 846 715 190
Calset Phospho-Tau (181P)	4 x 1.0 mL	07 357 044 190
PreciControl Phospho-Tau (181P)	6 x 1.0 mL	07 357 052 190
Elecsys® Total-Tau CSF[a)]	60 tests	08 846 685 190
Elecsys® Total-Tau CSF[b)]	100 tests	08 846 685 190
Calset Total-Tau	4 x 1.0 mL	07 357 010 190
PreciControl Total-Tau (181P)	6 x 1.0 mL	07 357 028 190

*a) for use of the **cobas e** 411 analyzer and the **cobas e** 601/602 modules;*
*b) for use on the **cobas e** 801 module and **cobas e** 402 module*

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