



INTRODUCING A NEW ERA FOR NEUROLOGICAL DIAGNOSTICS

DEVELOPING THE IDEAL TESTS
FOR
PHYSICIANS AND CLINICAL RESEARCH

Presented by Hugo Vanderstichele

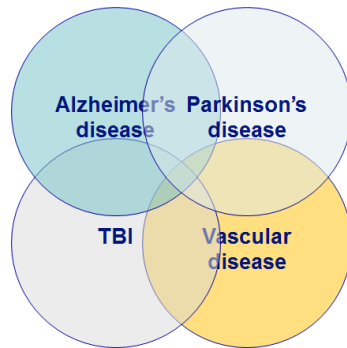
Date: 3/3/2017

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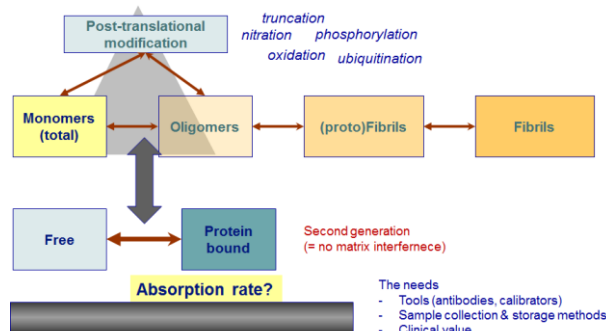
EUROIMMUN



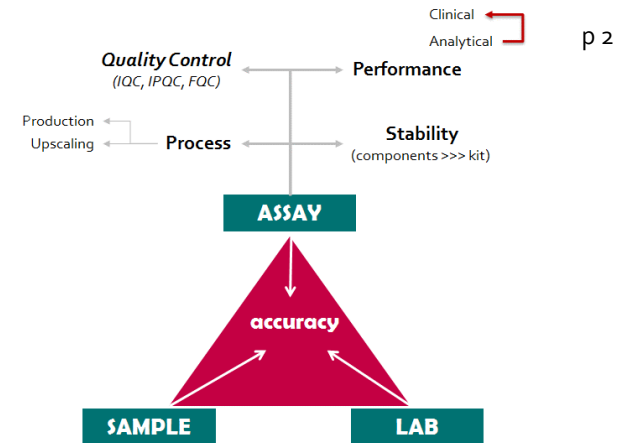
Some considerations from the field



Neurodegeneration
The need for protein **profiles**



Identify the correct protein **isoform**



Standardization required
at different levels

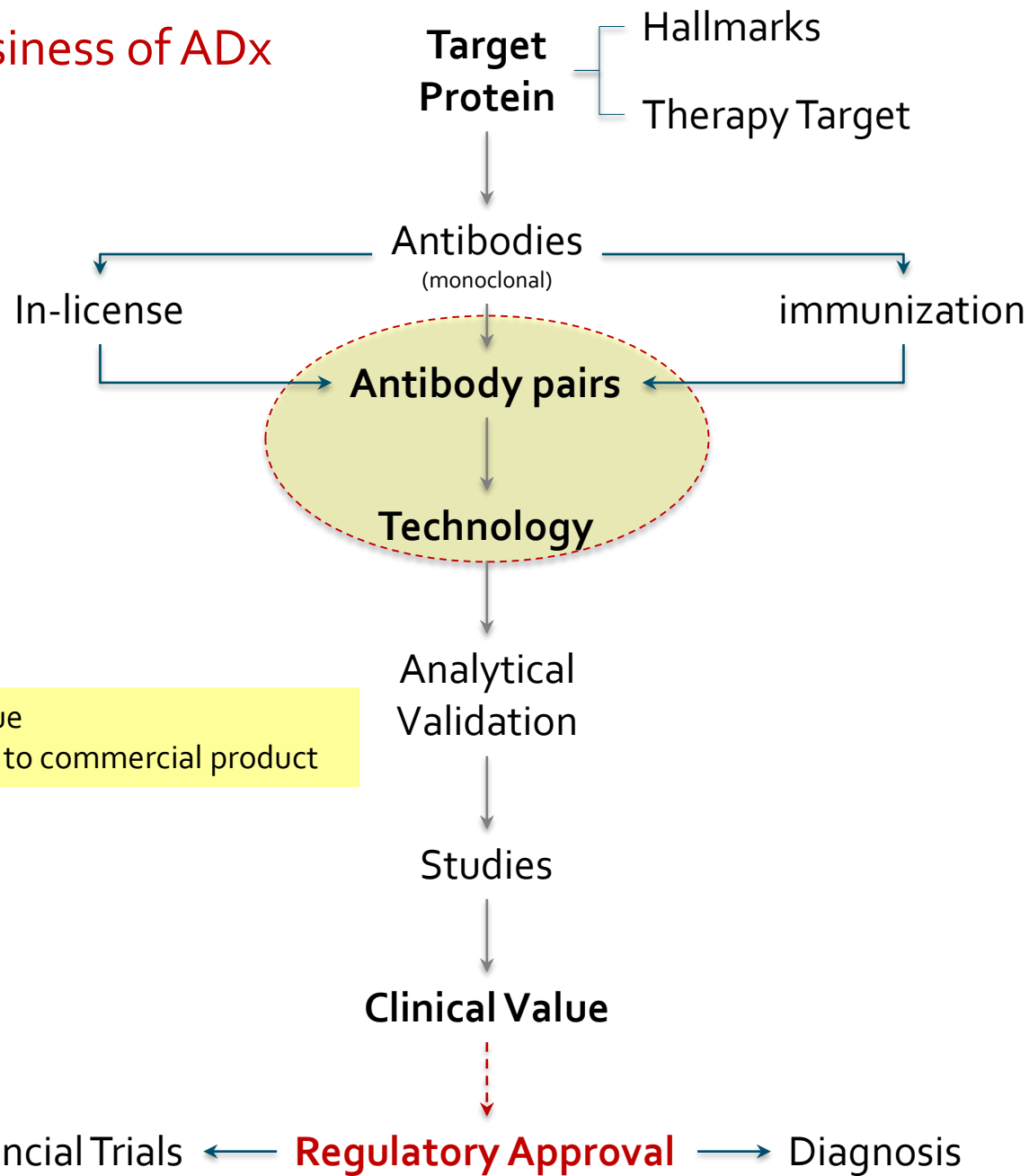
Regulatory approval
From RUO/IUO > IVD

Context of use

- Diagnosis
(... early, differential, prognosis)
- Clinical trials
(... enrichment, follow-up, dose-adjustment)

The core business of ADx

p 3



... from concept to value
... from research assay to commercial product



Neurodegeneration: Proteins and Hallmarks

The need for protein profiling (= multiplexing)

CE

RUO

p 4

Research

BRAIN

PLAQUES

TANGLES

LEWY BODIES

SYNAPSE LOSS

INFLAMMATION

OXIDATIVE
STRESS

Risk factors

CSF

A β ₁₋₄₂

A β N

A β ₁₋₄₀

A β ₁₋₃₈

TAU

NF-L

P-TAU_{181P}

(p) NF-H

P-TAU_{231P}

α -Synuclein

Oligo-Synuclein

P-Synuclein

Neurogranin *TruncP75*

BACE-1

SNAP-25

APOE₄

Pan APOE

BLOOD

A β ₁₋₄₂

A β ₁₋₄₀

A β ₁₋₃₈

TAU

(p) NH-H

α -Synuclein

Oligo-Synuclein

Neurogranin *TruncP75*

BACE-1

APOE₄

Pan APOE

Tau isoforms



ADx INSIDE: THE ADx mAbs & ASSAYS FIT A BROAD RANGE OF TECHNOLOGY PLATFORMS



From high-end Lab environments to flexible POC Centers



EUROIMMUN



Quanterix

Simoa HD-1 Analyzer



EUROIMMUN



Mitsubishi International Corporation

PATHFAST®

Point-of-Care Immunoassay Analyzer



The need for regulatory approval

Collaborative efforts required

Journal of Alzheimer's Disease 55 (2017) 19–35
DOI 10.3233/JAD-160573
IOS Press

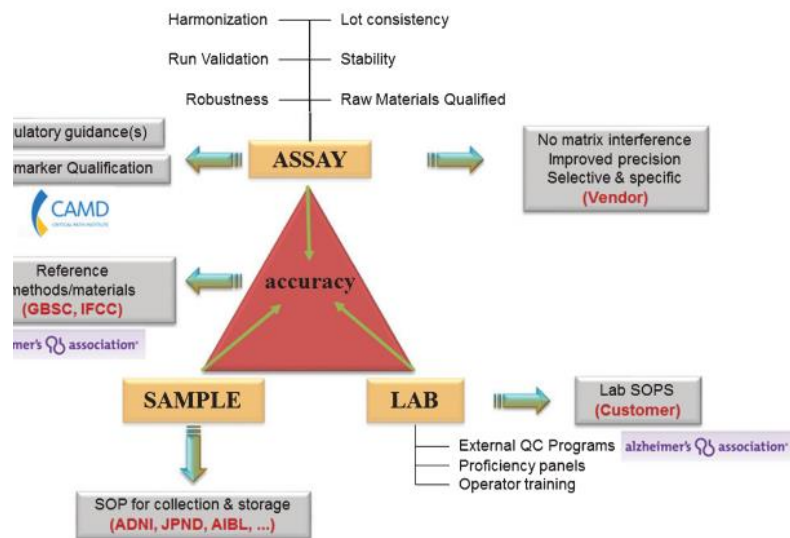
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Review

Cerebrospinal Fluid Biomarkers for Alzheimer's Disease: A View of the Regulatory Science Qualification Landscape from the Coalition Against Major Diseases CSF Biomarker Team

Stephen P. Amerić^{a,*}, Richard Batrla-Utermann^b, Laurel Beckett^c, Tobias Bittner^b, Kaj Blennow^d, Leslie Carter^e, Robert Dean^f, Sebastiaan Engelborghs^g, Just Genius^e, Mark Forrest Gordon^h, Janice Hitchcock^f, June Kaplowⁱ, Johan Luthmanⁱ, Richard Meibach^j, David Raunig^k, Klaus Romero^a, Mahesh N. Samtani^l, Mary Savage^m, Leslie Shaw^a, Diane Stephenson^a, Robert M. Umek^o, Hugo Vanderstichele^p, Brian Willis^f and Susan Yule^q

Global Initiatives Focused on AD CSF Biomarkers



Journal of Alzheimer's Disease 53 (2016) 1121–1132
DOI 10.3233/JAD-160286
IOS Press

1121

Improved SOPs collection & storage

Optimized Standard Operating Procedures for the Analysis of Cerebrospinal Fluid A β ₄₂ and the Ratios of A β Isoforms Using Low Protein Binding Tubes

Hugo Marcel Johan Vanderstichele^{a,*}, Shorena Janelidze^b, Leentje Demeyer^a, Els Coart^c, Erik Stoops^a, Victor Herbst^d, Kimberley Mauroo^a, Britta Brix^d and Oskar Hansson^{b,e}

Collaborations: Lund University (S), VUMC (NL)

Journal of Alzheimer's Disease 49 (2016) 187–199
DOI 10.3233/JAD-150511
IOS Press

187

Harmonization between studies

Transferring Cut-off Values between Assays for Cerebrospinal Fluid Alzheimer's Disease Biomarkers

Leandro García Barrado^a, Els Coart^{b,*}, Hugo M.J. Vanderstichele^c and Tomasz Burzykowski^{a,b}

Journal of Alzheimer's Disease xx (20xx) x–xx
DOI 10.3233/JAD-160298
IOS Press

1

Automation = better precision

Performance Evaluation of an Automated ELISA System for Alzheimer's Disease Detection in Clinical Routine

Davide Chiasserini^a, Leonardo Biscetti^a, Lucia Farotti^b, Paolo Eusebi^a, Nicola Salvadori^a, Viviana Lisetti^a, Francesca Baschieri^b, Elena Chipi^a, Giulia Frattini^a, Erik Stoops^c, Hugo Vanderstichele^c, Paolo Calabresi^{b,d} and Lucilla Parnetti^{a,b,*}

Collaborations: University of Perugia, University of Leuven (B)

Reference materials needed

Clinica Chimica Acta xxx (2016) xxx–xxxx



Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/clinchim



CSF A β _{1–42} – an excellent but complicated Alzheimer's biomarker – a route to standardisation

Julia Kuhlmann^a, Ulf Andreasson^{b,c}, Josef Pannee^{b,c}, Maria Bjerke^{b,c}, Erik Portelius^{b,c}, Andreas Leinenbach^d, Tobias Bittner^d, Magdalena Korecka^e, Rand G. Jenkins^f, Hugo Vanderstichele^g, Erik Stoops^g, Piotr Lewczuk^{h,i}, Leslie M. Shaw^e, Ingrid Zegers^a, Heinz Schimmel^a, Henrik Zetterberg^{b,c,j}, Kaj Blennow^{b,c,*}, on behalf of the IFCC Working Group on Standardization of CSF proteins (WG-CSF)

Collaboration: IDDI (B)



Journal of Alzheimer's Disease 53 (2016) 1523–1538
DOI 10.3233/JAD-160227
IOS Press

1523

The need for progression markers

The Cerebrospinal Fluid Neurogranin/BACE1 Ratio is a Potential Correlate of Cognitive Decline in Alzheimer's Disease

Ann De Vos^a, Hanne Struyfs^b, Dirk Jacobs^a, Erik Fransen^c, Tom Klewansky^d, Ellen De Roeck^{b,e},
Caroline Robberecht^{f,g}, Christine Van Broeckhoven^{f,g}, Charles Duyckaerts^d,
Sebastiaan Engelborghs^{b,h} and Eugeen Vanmechelen^{a,*}

CSF A β ratios correlate better with A β PET imaging

ANNALS
of Clinical and Translational Neurology

Open Access



RESEARCH ARTICLE

CSF A β 42/A β 40 and A β 42/A β 38 ratios: better diagnostic markers of Alzheimer disease

Shorena Janelidze¹, Henrik Zetterberg^{2,3}, Niklas Mattsson^{1,4}, Sebastian Palmqvist^{1,5},
Hugo Vanderstichele⁶, Olof Lindberg¹, Danielle van Westen^{7,8}, Erik Stomrud^{1,4}, Lennart Minthon^{1,4},
Kaj Blennow², for the Swedish BioFINDER study group & Oskar Hansson^{1,4}



Commercial products from EUROIMMUN

Example of a validation report

Antigen detection

Available product	Description	CSF	Plasma	Order no.
Beta-Amyloid (1-38) ELISA	Test kit for the quantitative determination of beta-amyloid (1-38) as an additional diagnostic tool in suspected clinical amyloid pathology of the brain.	■	■	EQ 6501-9601-L* EQ 6501-9601*
Beta-Amyloid (1-40) ELISA	Test kit for the quantitative determination of beta-amyloid (1-40). Can be used to calculate beta-amyloid (1-42)/beta-amyloid (1-40) as an additional diagnostic tool in suspected amyloid pathology of the brain.	■	■	EQ 6511-9601-L EQ 6511-9601*
Beta-Amyloid (1-42) ELISA	Test kit for the quantitative determination of beta-amyloid (1-42) as an additional diagnostic tool in suspected clinical amyloid pathology of the brain.	■	■	EQ 6521-9601-L EQ 6521-9601*
Total-Tau ELISA	Test kit for the quantitative determination of total tau for the diagnosis of neuronal apoptosis.	■		EQ 6531-9601-L
Phosphorylated-Tau ELISA	P-tau (T181) determination is an additional diagnostic tool in suspected tauopathy in the brain of patients with neurodegenerative disorders.	■		coming soon
Beta-Amyloid Control Set	CSF sample set with target values. Can be used for on-site training as well as regular internal quality control of amyloid and tau measurements.	■		CK 6500-0502-L*
ApoE4 ELISA	Test kit for ApoE4 protein determination. Measureable ApoE4 protein concentrations indicate at least one ApoE allele that is a risk factor for the development of Alzheimer's disease.	■	■	coming soon
Pan-ApoE ELISA	Test kit for the quantitative determination of pan-ApoE.	■	■	coming soon
BACE1 ELISA	Test kit for the determination of BACE1 protein concentration.	■		EQ 6541-9601-L*
Neurogranin (trunc P75) ELISA	Test kit for the quantitative determination of neurogranin.	■		EQ 6551-9601-L*
pNf-H ELISA	Test for the quantitative determination of phosphorylated neurofilament heavy chain. Can be used as an additional tool for the early diagnosis of motoneuronal diseases like amyotrophic lateral sclerosis.	■	■	EQ 6561-9601*
Alpha-Synuclein ELISA	Alpha-Synuclein is a measure for Lewy body pathology in the brain.	■		coming soon

*on request and for research use only

Molecular diagnostics

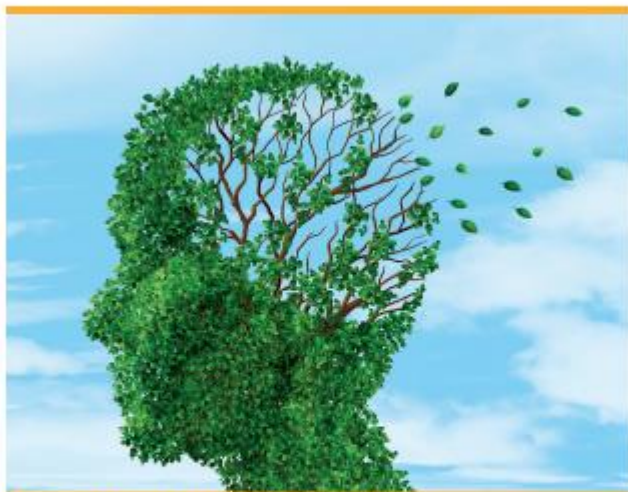
Available product	Description	Full blood sample	Order no.
EUROArray APOE Direct	Test system for molecular genetic diagnostics of Alzheimer's disease and type III hyperlipoproteinemia, as well as other diseases associated with the alleles ε2, ε3 and/or ε4 of the APOE gene.	■	MN 5710-0803-V MN 5710-0505-V MN 5710-1005-V MN 5710-2005-V

VALIDATION REPORTS

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Medizinische
Labor Diagnostika
AG

VALIDATION REPORT

Beta-Amyloid (1-42) ELISA

Addendum 1 – References

Addendum 2 – Certificate of the Beta-Amyloid (1-42) calibrator

Addendum 3 – Preparation of CSF controls; preparation of calibrators and validation controls

Addendum 4 – Declaration of Conformity and Certificate