IRMM/IFCC
Project Overview

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Niklas’ slide on the different players in the AD biomarker standardization field:

Reference methods
GBCS
IFCC working group

Use reference methods to set levels in reference materials
• Pilot batches by GBCS with partners including the IFCC working group
• Large-scale production by IRMM

Supply reference material to assay producers by IRMM (non-profit)

Certification of methods and materials by IFCC

Collaboration with other research consortia

The QC program
Monitor and evaluate the progress of the global standardization efforts
What is IRMM?

One of the seven institutes of the Joint Research Centre (JRC), a Directorate-General of the European Commission (EC)

One of the world's leading reference material producers, as well as a provider of reference measurement data (non-profit)
What is IRMM?

Operates four European Union Reference Laboratories (around 300 employees). Its management system is certified according to ISO 9001, ISO 14001 and OHSAS 18001 and its units hold several accreditations.

Collaborates with several other metrology institutes, including NIST (National Institute of Standards and Technology).
IRMM – role in AD biomarker standardization project?

They have made a formal decision to:

(i) assist in the development of reference materials for CSF Aβ42, T-tau and P-tau

(ii) produce and provide the final materials

(iii) assist in the development of reference methods for the analytes.
IRMM – role in AD biomarker standardization project?

Project manager at IRMM:

Dr Ingrid Zegers, who is also a part of the IFCC working group on CSF biomarkers
What is IFCC?

The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) is a worldwide, non-political organization for clinical chemistry and laboratory medicine.
What is IFCC?

Goals:

(i) global standard setting in clinical laboratory procedures in collaboration with other international organizations,

(ii) supporting its members through scientific and educational endeavor, and

(iii) providing a series of congresses, conferences and focused meetings
Has the power to certify reference materials and methods

Initiates projects
August, 2011: Project proposal on the development of reference materials and methods for AD biomarkers submitted by the Swedish Society for Clinical Chemistry

October, 2011: Project approved by IFCC (the field is mature!)

May, 2012: Working group formed by the Scientific Division
CSF-Proteins (WG-CSF)

Membership

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<td>A. Larsson</td>
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Companies can be represented in the WG if they are corporate members of IFCC
Objectives of the IFCC WG-CSF

(i) to develop an international reference material for cerebrospinal fluid (CSF)

(ii) to establish reference methods for the key measurands for assignment of values to the reference material

The work will be evaluated on a yearly basis by the scientific division at IFCC
Candidate reference methods will be developed by GBSC members, the IFCC WG and other research teams.

Protocols can be published and also submitted to the IFCC WG for evaluation.

The scientific division at IFCC gives advice on methods that seem to fulfil reference method standards and can submit nominations for IFCC certification (independent validation essential).
Outline of project – certified reference materials (CRMs)

Candidate reference materials developed by GBSC, IFCC WG, other teams

Material selection

Feasibility study (collection, processing, characterization, commutability)

Homogeneity study

Storage

Processing

Interim transport and storage

Material collection

Short-term stability study

Long-term stability study

Value assignment

Commutability study

Follow-up stability monitoring of CRM

Assessment by experts

Documentation

CRM Distribution and Sales
Current status and timeline

(i) A number of candidate SRM-based reference methods for Aβ42 in place – round robin and further harmonization efforts in progress

(ii) Tau approaches need to start

(iii) Candidate reference materials will be produced and evaluated during autumn

Suggestion: submit a candidate reference method for Aβ42 for evaluation by the scientific division at IFCC before end of 2012?
Themed issue of Biomarkers in Medicine in August 2012

Examples of titles:
- What is a certified reference material?
- Reference measurement procedures for Alzheimer’s disease cerebrospinal fluid biomarkers – definitions and approaches
- Analytical aspects of molecular AD biomarkers
- Proficiency testing programs for Alzheimer’s disease cerebrospinal fluid biomarkers
- Determining cut-points for Alzheimer’s disease biomarkers: statistical issues, methods and challenges
- Neurochemical Dementia Diagnostics: an ISO 15189 perspective
- Clinical use of CSF biomarkers in Alzheimer’s disease
- Recommendations to standardize pre-analytical confounding factors in Alzheimer’s and Parkinson’s disease CSF biomarkers: an update.
- Upcoming candidate CSF biomarkers for Alzheimer’s disease
- Plasma biomarkers for AD: much needed but tough to find
Outstanding issues and further discussion...

Not even the gold standard is gold:

Amino acid analysis of the same internal Aβ1-42 standard at two independent laboratories 20% off...
Acknowledgments

alzheimer’s association®

the compassion to care, the leadership to conquer