

# 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

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the compassion to care, the leadership to conquer

  
Institute for Reference  
Materials and Measurements

  
**IFCC**  
International Federation  
of Clinical Chemistry  
and Laboratory Medicine

# 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 A $\beta$ 42, 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?

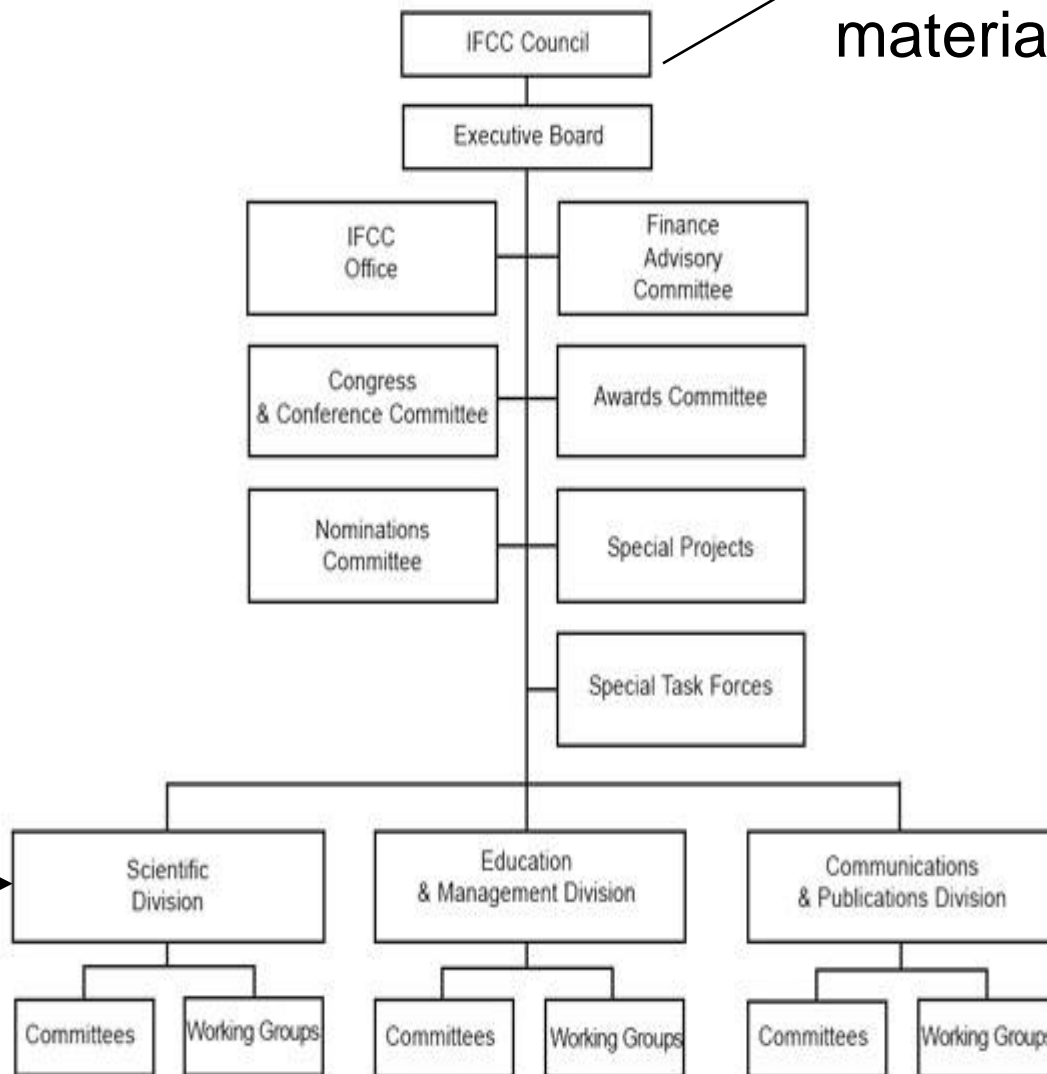
## Goals:

- (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

Name	Position	Country	Term	Time in Office
K. Blennow	Chair	SE	1st	2012 06 - 2014 12
A. Larsson	Member	SE		
M. Korecka	Member	US		
P. Lewczuk	Member	DE		
L.M. Shaw	Member	US		
I. Zegers	Member	BE		
H. Zetterberg	Member	SE		

*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

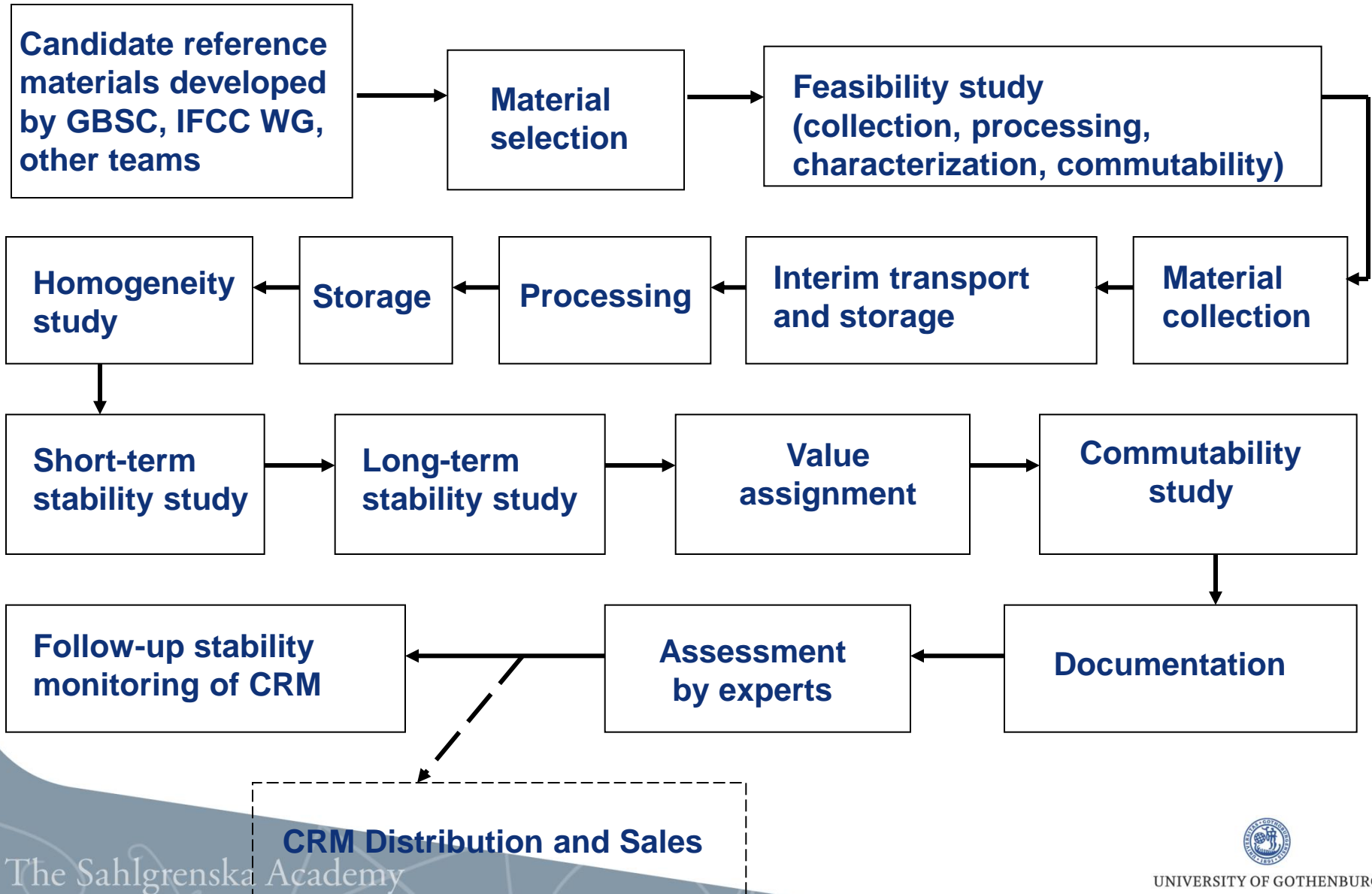
# Outline of project - methods

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)



# Current status and timeline

- (i) A number of candidate SRM-based reference methods for A $\beta$ 42 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 A $\beta$ 42 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 A $\beta$ 1-42 standard at two independent laboratories 20% off...

# Acknowledgments

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